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AIR POLLUTION ASPECTS OF ORGANIC CARCINOGENS

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Litton Systems, Incorporated
Bethesda, Maryland

September 1969

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AIR POLLUTION ASPECTS
OF
ORGANIC CARCINOGENS

Prepared for the
National Air Pollution Control Administration
Consumer Protection & Environmental Health Service
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FOREWORD

As the concern for air quality grows, so does the concern over the less ubiquitous but potentially harmful contaminants that are in our atmosphere. Thirty such pollutants have been identified, and available information has been summarized in a series of reports describing their sources, distribution, effects, and control technology for their abatement.

A total of 27 reports have been prepared covering the 30 pollutants. These reports were developed under contract for the National Air Pollution Control Administration (NAPCA) by Litton Systems, Inc. The complete listing is as follows:

Aeroallergens (pollens)
Aldehydes (includes acrolein and formaldehyde)
Ammonia
Arsenic and Its Compounds
Asbestos
Barium and Its Compounds
Beryllium and Its Compounds
Biological Aerosols (microorganisms)
Boron and Its Compounds
Cadmium and Its Compounds
Chlorine Gas
Chromium and Its Compounds (includes chromic acid)
Ethylene
Hydrochloric Acid
Hydrogen Sulfide
Iron and Its Compounds
Manganese and Its Compounds
Mercury and Its Compounds
Nickel and Its Compounds
Odorous Compounds
Organic Carcinogens
Pesticides
Phosphorus and Its Compounds
Radioactive Substances
Selenium and Its Compounds
Vanadium and Its Compounds
Zinc and Its Compounds

These reports represent current state-of-the-art literature reviews supplemented by discussions with selected knowledgeable individuals both within and outside the Federal Government. They do not however presume to be a synthesis of available information but rather a summary without an attempt to interpret or reconcile conflicting data. The reports are necessarily limited in their discussion of health effects for some pollutants to descriptions of occupational health exposures and animal laboratory studies since only a few epidemiologic studies were available.

Initially these reports were generally intended as internal documents within NAPCA to provide a basis for sound decision-making on program guidance for future research activities and to allow ranking of future activities relating to the development of criteria and control technology documents. However, it is apparent that these reports may also be of significant value to many others in air pollution control, such as State or local air pollution control officials, as a library of information on which to base informed decisions on pollutants to be controlled in their geographic areas. Additionally, these reports may stimulate scientific investigators to pursue research in needed areas. They also provide for the interested citizen readily available information about a given pollutant. Therefore, they are being given wide distribution with the assumption that they will be used with full knowledge of their value and limitations.

This series of reports was compiled and prepared by the Litton personnel listed below:

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ABSTRACT

Epidemiological studies indicate that air pollution may play a role in lung cancer induction. Certain organic carcinogens, normally present in polluted air, particularly benzo(a)pyrene, have been shown to increase tumor incidence in experimental animals. In addition, animal studies indicate that other organic compounds may have synergistic or antagonistic effects. No information has been found on the effects of organic carcinogens on plants or materials.

Organic carcinogens fall into three main categories--polynuclear aromatic hydrocarbons, polynuclear heterocyclic and oxygenated compounds, and alkylating agents. The major emission sources of organic carcinogens, particularly of polynuclear aromatic hydrocarbons, are heat-generation sources, such as burning coal, oil, and gas; refuse burning; motor vehicle exhaust; and industrial processes. Of these, heat generation accounts for more than 85 percent of the polynuclear aromatic hydrocarbons generated, while the other three sources each account for about 5 percent of the total.

In 1966, the average ambient air concentration of benzo(a)pyrene in the United States was approximately 0.003 ug/m^3 for urban areas and 0.0003 ug/m^3 for nonurban areas. Data indicate that benzo(a)pyrene represents only a small percentage of the total amount of polynuclear aromatic hydrocarbons found in the atmosphere.

Abatement methods for organic carcinogens are presently being studied under the hydrocarbon control programs.

The costs of premature death and the associated costs of treatment and burial for lung cancer ascribable to air pollution have been estimated. No information has been found on the economic costs of the abatement of organic carcinogen air pollution.

Methods of analysis are available which involve the use of extraction and chromatographic techniques for separation of the compounds followed by analysis with spectral methods.

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1. INTRODUCTION

According to some estimates,[12,108,138] the mortality rate from lung cancer has increased about 30 times since 1900. This alarming increase has occasioned studies concerning the cause of cancer. A portion of the organic material present in the atmosphere, generally as suspended particulates, has been identified as carcinogenic to experimental animals. These organic carcinogens have been identified in the atmosphere of virtually all large cities in which surveys have been conducted. It is true, however, that in no case has a suspected organic carcinogen been demonstrated to produce lung cancer in humans.

According to Sawicki,[188] the composition of the urban atmosphere is as yet (1967) undetermined, the vast majority of the constituents being unknown. Certain organic compounds present as particulates in the atmosphere have been identified, and several of these have been found to be carcinogenic to animals. There is also evidence that other organic compounds may be carcinogenic.

Although there is some question as to the carcinogenicity of selected compounds (such as those marked with an asterisk), the major classes of organic carcinogens are as follows:

Polynuclear Aromatic Hydrocarbons (PAH)
    Benzo(a)pyrene (BaP)
    *Benzo(e)pyrene
    Benz(a)anthracene
    Benz(e)acephenanthrylene
    Benzo(b)fluoranthene

Benzo(j)fluoranthene
*Chrysene
Dibenzo(e,l)pyrene
Dibenzo(a,h)pyrene
Indeno(1,2,3-cd)pyrene
1,2-Benzanthracene

Polynuclear Aza-Heterocyclic Compounds
  Dibenz(a,h)acridine
  Dibenz(a,j)acridine

Polynuclear Imino-Heterocyclic Compounds

Polynuclear Carbonyl Compounds
  *7H-Benz(de)anthracen-7-one

*Alkylating Agents
  Aliphatic and olefinic epoxides
  Peroxides
  Lactones

The carcinogenicity of the above organic compounds has been established through laboratory experimentation by many investigators. It should be noted that, in many experiments, A-strain mice particularly susceptible to tumor development were used, and only in two studies was inhalation used as the route of administration.[125]

The presence of substituent groups, particularly alkyl groups, on some of these or other PAH compounds can cause a profound change in their carcinogenic activity.[188] Thus, while both benz(a)acridine and benz(c)acridine are inactive when placed on the skin of mice, their 7-methyl derivatives are very active (rated similar to BaP in carcinogenic activity).[228] Some of the other methyl derivatives of these two compounds are also active.[228] Furthermore, whereas chrysene was found inactive on the subcutaneous tissue of mice, the 4-, 5-, and 6-methyl derivatives were all active.[9]

The major source of atmospheric organic carcinogens is the incomplete combustion of organic matter.[91] A secondary source is the photochemical decomposition of noncarcinogenic organic compounds into more active compounds. Incomplete combustion, which generates organic carcinogens, occurs in the process of heat generation, refuse burning, operation of motor vehicles, and several industrial processes. Of the compounds generated, the most extensively studied are the polynuclear aromatic hydrocarbons (PAH), particularly benzo(a)-pyrene (also known as 3,4-benzopyrene or BaP), which is considered the carcinogen most active to animals. Much of the literature pertaining to the air pollution aspects of organic carcinogens concentrates on the compound BaP, due in part to its high relative carcinogenicity, and also in part to the fact that its identification and quantitative determination in air are relatively simple. Information concerning the other known or suspected carcinogens is limited or nonexistent, and in the words of Sawicki,[188] "We have no knowledge as to whether the members of this great number of unknown trace chemicals are innocuous, beneficial, or harmful to life in the concentrations at which they are present in the various nonurban, industrial, and urban atmospheres."

1.1 Types of Organic Carcinogens

1.1.1 Polynuclear Aromatic Hydrocarbons (PAH)

The majority of polynuclear aromatic hydrocarbons (PAH) in our environment evolve from high-temperature reactions under pyrolytic conditions during incomplete combustion of organic matter. The formation of PAH during such processes occurs in two distinct types of reactions, pyrolysis and pyrosynthesis. At temperatures above 400° to 500°C, organic components are partially cracked into smaller, unstable molecules (pyrolysis). These fragments, mostly radicals, recombine into larger, thermodynamically favored and relatively stable PAH and heterocyclic hydrocarbons (pyrosynthesis).[103]

Badger and his co-workers have studied the pyrosynthesis of PAH.[10,11] Their original working hypothesis is illustrated in Figure 2 in the Appendix. From these data and from information acquired by other investigators,[103] the following concept has been formulated: the temperature that exists during the burning of organic matter easily breaks single carbon and carbon-hydrogen bonds to yield free radicals. These radicals combine and are dehydrogenated to form aromatic ring systems that are relatively stable; only the carbon-hydrogen bonds of these components are broken to any significant extent. Long-chain paraffins, widely found in fuels and plants, serve as special precursors of PAH. Badger's original concept of PAH formation was verified by extensive, carefully designed and carefully executed experiments utilizing ^{14}C-labeled precursors. Figure 3 in the Appendix summarizes the steps of BaP pyrosynthesis as they are suggested from the experimental findings. This concept can be extended to include hydrocarbons with uneven carbon numbers since methane also serves as a precursor of PAH.[25]

Pyrolysis experiments like these were conducted in a nitrogen atmosphere and have been criticized for not accurately reflecting the conditions that prevail during the actual burning of organic matter. As Hoffmann and Wynder[103] point out, the fact remains that these studies agree qualitatively with actual burning conditions of organic matter, and the cited studies were conducted primarily to discover the major precursors and pathways for the pyrosynthesis of PAH rather than to compile quantitative data on pyrosynthesis.

In studies of actual burning of organic matter, a reducing atmosphere exists around and/or inside the burning cone, as well as inside the combustion chamber. Newsome and Keith[157] found this type of reducing atmosphere in the inner cone of a cigarette, where it consists partially of hydrogen (8.2 volume percent), carbon monoxide (11.8 percent), and methane (1.3 percent), and contains only traces of oxygen (1.4 percent). Gasoline engine exhaust gases generated during idling may contain up to 18 volume percent carbon monoxide, 2 percent volatile hydrocarbons, and traces of hydrogen. The concentrations of carbon monoxide, methane, and hydrogen and the absence or very low concentrations of oxygen in the combustion products indicate the existence of a reducing atmosphere around and/or inside the flame or combustion chamber. A reducing atmosphere is essential for pyrosynthesis of PAH.

As indicated in Figure 3 in the Appendix, other PAH can be formed by the preceding mechanisms. Long and his co-workers[145] at the University of Birmingham have also shown that many PAH are formed during incomplete combustion of ethylene and ethane. The structures of several representative PAH which have been identified in urban air are shown in Figure 4 in the Appendix. Not all of the PAH, however, are carcinogenic (see Table 1).

In addition to the PAH in our environment that envolves from incomplete combustion of organic matter, a small portion of it may derive from thermic or catalytic cracking of organic components. The chemical mechanisms leading to the formation of trace amounts of PAH by cracking are similar to those occurring during incomplete combustion.

PAH occur in the atmosphere primarily as adsorbed compounds on soot particles. The biological effect of the carcinogenic agents is critically related to the physical characteristics of the particle. Particle size primarily determines the extent of penetration into the tracheobronchial tree.[119,121] To a great extent, particle size also governs the rate and extent of the elution of carcinogenic hydrocarbons from the soot particles on which they are adsorbed.[70]

TABLE 1

CARCINOGENICITY AND ANTICARCINOGENICITY OF SOME COMPOUNDS PRESENT IN POLLUTED AIR[28,117]

Compound	Carcinogenicity[a] Ref. 117	Carcinogenicity[a] Ref. 28	Anticarcinogenicity Ref. 28
Benzanthracene	+	+	+
Benzo(e)pyrene	+	-	+
Benzo(a)pyrene	+++	+++	
Anthanthrene	-	-	-
Perylene	-	-	+
Benzo(g,h,i)perylene	-	-	-
Benzo(k)fluoranthene	-	-	+
Benzo(b)fluoranthene	++	++	
Benzo(j)fluoranthene	++		
Fluoranthene	-	-	
Indeno(1,2,3-cd)pyrene	+		
Anthracene		-	+
Phenanthrene		-	-
Pyrene	-	-	+
Benz(m,n,o)fluoranthene		-	+
Chrysene[b]	+	+	+
Benzo(c)acridine		+	+
Benzo(a)fluorene		-	+
Fluorene		-	-
Coronene	-	-	-
Benz(a)carbazole		+	+
2-Naphthol		-	-

[a] Inactive: -; weakly active: +; moderately active: ++; strongly active: +++.

[b] Carcinogenic properties may be due to the impurity 5H-benzo(b)carbazole present in "commercial pure" chrysene.[246]

See Section 2.1.2 for further discussion of particle size.

1.1.2 Polynuclear Heterocyclics and Oxygenated Compounds

Large quantities of aza-heterocyclic compounds are found in the compounds contained in some air pollution source effluents,[197] in very low concentrations in automotive exhaust fumes,[196] and in moderate concentrations in the air.[214] Sawicki[188] states that many of these compounds and some others have never been tested for carcinogenic activity; dibenz(a,h)-acridine and dibenz(a,i)acridine (see Figure 5 in the Appendix), however, are carcinogenic. Many polynuclear carbazoles have been found to be carcinogenic.[14] In general, however, information is scanty in this area.

In regard to polynuclear carbonyl compounds, Hoffmann and Wynder[103] note that, in theory, many known nonvolatile "oxygenated substances" may exist in our respiratory environment. However, very few chemical studies concerning these compounds have been reported. This is surprising, since many neutral "oxygenated" compounds have been found in tobacco smoke.[287]

The paucity of chemical data in this area may be a consequence of a lack of biological information on the subfractions containing oxygenated substances.

1.1.3 Alkylating Agents

Common alkylating agents found in the atmosphere include epoxides, peroxides, and lactones.

Certain epoxides and peroxy compounds have been shown to be carcinogenic,[122,268,269] as well as to have other physiological effects.[119] A recent source of these types of compounds is the universal use of liquid fuels, such as gasoline and diesel fuel, in the internal combustion engine.[119,186] In the unburned state, these liquid fuels are highly reactive and when volatilized, undergo oxidation in the presence of oxides of nitrogen in a photochemical reaction. The reaction products consist of a broad group of peroxides, including compounds with epoxidic linkages. The unburned gasoline and other exhaust products emitted from automobiles contain significant quantities of ethylene, propylene, butene, and other unsaturated hydrocarbons. Under certain meteorological conditions, these vapors react in the presence of sunlight and oxides of nitrogen to form a broad spectrum of hydrocarbon oxidation products.

Interest in compounds belonging to this group has centered primarily around the formation of epoxides because of the demonstrated carcinogenic potency of certain classes of these compounds.

Sato and Cvetanovic[186] studied the decomposition of unsaturated hydrocarbons; the products of decomposition following photochemical reaction include compounds with epoxidic linkages. A typical reaction is shown in Figure 6 in the Appendix. These reactions account for the major decomposition products, which include formaldehyde and acetone as well as epoxides. Some of the latter compounds belong to the group of experimentally verified carcinogens. Apparently, significant quantities of epoxides are produced.

The concentration of hydrocarbons in the air from auto exhaust is about 3.4 ppm.[119] Of this amount, 1 ppm is made up of saturated hydrocarbons, and the remainder consists of olefins associated with 0.05 ppm diolefins. Ethylene, constituting half of the olefins produced, is of special significance. When the automotive exhaust is exposed to light and air, photochemical reactions occur which destroy 56 percent of the total amount of hydrocarbons in a 2-hour interval. Two-thirds of the hydrocarbons which are destroyed are olefinic (excluding ethylene), i.e., olefins which are known to give a 17 percent epoxide yield. Thus, 6 percent of the total hydrocarbons emitted from the exhaust are transformed to epoxides of the type that have been found to be carcinogenic to experimental animals.[28] The controlled reaction is equivalent to 2 hours of exposure to photochemical reactions that occur naturally in the Los Angeles atmosphere. The epoxide concentrations determined are conservative.[119]

1.2 Organic Carcinogens as Cocarcinogens or Anticarcinogens

Little information is available regarding the synergistic or antagonistic effects of organic carcinogens. However, the limited animal studies available have demonstrated that organic carcinogens do play a role as cocarcinogenic or anticarcinogenic agents. There are data that suggest that phenols and some long-chained hydrocarbons are cocarcinogenic.[175,228]

Table 1 in Section 1.1.1 shows some PAH that were reported by Kotin and Falk[121] to have anticarcinogenic activity. These authors also presented data that demonstrated that the carcinogenic properties of dibenz(a,h)anthracene, a strong carcinogen, can be strongly inhibited by the dihydro- and the hexahydro-derivatives of dibenz(a,h)anthracene, as well as with benz(a)anthracene and phenanthrene. Several other authors have reported that a weak carcinogen or noncarcinogen can inhibit the activity of normally potent chemically related carcinogens.[40,126,132,237]

2. EFFECTS

According to Pybus,[165] cancer has puzzled mankind since it was first recognized in the fourth century B.C. The first and most important observation of its cause was made by a London surgeon, Percival Pott, who in 1775 described cancer of the scrotum in chimney sweeps; he decided it resulted from the soot lodged in the crevices of the skin of the male genitals.[165] This apparent causal relationship between soot and skin cancer led to attempts to produce cancer in animals by painting tar on their skin. The earliest experiments, performed about 1889, failed because they were conducted on resistant animals or because not enough time was allowed for the cancer to develop. Thus, the demonstration that soot or tar was actually responsible for this form of cancer remained unproved until 1915, when skin cancer was produced in a rabbit by means of repeated applications of extracts of tar.[165]

After World War I, British investigators, under the leadership of Sir Ernest Kennaway, demonstrated by persistent and tedious experimentation that skin cancer could be induced in mice by coal tar. Fractionation of the tar to isolate the active ingredients led to the discovery that the tumor-producing constituents were also highly fluorescent. Thus, examination of fractions for fluorescence guided the separations rather than lengthy animal tests, and rapid progress was made. A discovery followed shortly: certain PAH, such as the now familiar BaP contained in the tar are responsible in part for the tar's carcinogenic effect.[165]

Numerous studies have demonstrated a worldwide increase in the frequency of and mortality from lung cancer. These investigations leave little doubt that the apparent increased incidence of lung cancer is both real and, at least until very recently, progressive. Interest in this lung cancer increase has sparked many biological and medical investigations. Some of the studies have been concerned with the effect of air pollution and/or smoking. Many of the studies relating air pollution to cancer in humans are epidemiological. As already noted, airborne carcinogens have been the subject of considerable study in the laboratory.

Although cigarette smoking has been a widely publicized issue for more than a decade, it is generally agreed, however, that a history of cigarette smoking is causally related to the risk of developing lung cancer. Any meaningful discussion of the relation of lung cancer to cigarette smoking is clearly beyond the scope of a survey directed toward national air pollution control. A review of this subject by Rigdon and Kirchoff[171] covers the years 1930 through 1960. More recent articles have dealt with the chemical composition of tobacco smoke,[235,288] the mechanism of carcinogenic action of tobacco smoke,[71] smoking and oral cancer,[226] smoking and cancer of the lung,[174] smoking and cancer of the urinary tract,[74] and retention of cigarette smoke by the lungs.[43] In addition, the U.S. Public Health Service has issued overall views of smoking and health.[95,232]

A related area which is pertinent to this survey is the impact of smoking as compared with air pollution on development of lung cancer. The reports seem to indicate that the joint effect of cigarette smoking and air pollution is additive rather than multiplicative; however, the evidence is still inconclusive.[23,24,247,285]

2.1 Effects on Humans

Although no suspected organic carcinogen has been proved experimentally to cause lung cancer in humans,[3] an apparent association has been shown between air pollution and human mortality rates from lung cancer. Furthermore, organic carcinogens have been shown to increase tumor activity in experimental animals. Data on experimental animals is presented in Section 2.2.

The increase in the absolute mortality resulting from cancer (especially of the lung) has been demonstrated in various parts of the world during the past half century. Kotin and Falk[119] indicated that this increased mortality has been characterized by the following: (1) greater susceptibility to lung cancer in urban than in rural residents; (2) greater incidence among individuals with a history of prolonged and excessive cigarette smoking; and (3) greater frequency of lung cancer in males than in females.

The increased incidence of lung cancer parallels the introduction of new etiological agents into the respiratory environment around the turn of the century.[119] Since lung cancer, as other neoplasms, is not likely to result from a single initiating or promoting experience, it is important to evaluate the pathogenic significance of polluted air. This evaluation is necessary both for the detection of carcinogens and the determination of the role of air pollution in relation to other environmental factors.[119]

Numerous investigations [37,42,49,51,60,61,88,102,119, 128,162,222,242,285,289] have indicated a higher incidence of lung cancer for urban residents than for rural residents. Studies relating smoking to lung cancer[55,56,87,88,153,219,284] also show the so-called "urban factor." After correcting for the differences in smoking habits between urban and rural residents in the United States, the rate of lung cancer was still 25 percent lower in rural areas.[88]

The nature and significance of the urban effect have not been specifically established. It may result from occupational differences, from rural patients' habit of obtaining improved medical care in the city and reporting as urban residents, from improved accuracy of cancer reporting in urban areas, or from a combination of these and other factors.

In 1964 Buck and Wicken[22] reported an association between the degree of air pollution and the incidence of lung cancer and bronchitis mortality in two areas of the Eston (England) urban district. However, Zeidberg _et al_.[294] reported (also in 1964) on a study of 9,313 individuals in Nashville, Tenn., in which they found no evidence of a relationship between air pollution and cancer morbidity rates.

Nevertheless, exposure to polluted air is a widely accepted explanation for the consistent observation of increased lung cancer incidence in urban populations. Epidemiological, physicochemical, and biological data are consistent with an etiological role for polluted atmosphere.

Kotin and Falk[121] cite the following evidence to support the contention that air pollution may be a significant factor in the pathogenesis of lung cancer:

(1) Carcinogenic agents have been identified and quantified in the polluted air of essentially every city in which they have been sought;

(2) Similarly, chemical compounds with known tumor-promoting properties have been identified and quantified in polluted urban air;

(3) The stability and survival of carcinogenic hydrocarbons in the atmosphere are compatible with inhalation and a postulated biological effect in those exposed;

(4) Carcinogenic agents, as well as noncarcinogenic respiratory epithelial irritants, occur in the atmosphere in a state compatible with host entry and tracheobronchial deposition;

(5) Alteration in function and structure of the respiratory epithelium of representative mammalian species has been demonstrated following exposure to a broad spectrum of these environmental irritants. The resulting changes appear to facilitate the biological action of carcinogenic agents; and,

(6) Bioassay by skin-painting and subcutaneous-injection techniques has established the carcinogenic properties of compounds identified in and extracted from polluted air. Exposure of both susceptible and resistant strains of mice to aerosols of synthetically reproduced polluted urban air has resulted in lung tumors in both strains.

Epidemiological studies of immigrants[5,49-51,61,62,85,148,167] indicate that air pollution may be an etiological factor which has long-term residual effects with a latent period of induction. British immigrants to South Africa had a higher incidence of mortality from lung cancer than the native white South Africans, who smoked even more than the immigrants.[50,51] This was observed in British immigrants who had resided in South Africa even for 20 or more years. Similar studies indicate that immigrants to New Zealand,[61,62] Austria,[51] Israel,[167] and Mexico[148] showed a greater pattern of lung cancer than was found in their new area of residence. In contrast, Norwegian immigrants who moved to the United States, where the air pollution was greater than in their home country, had a cancer rate higher than native Norwegians but less than the native Americans.[85] It has been further observed in the United States[86] that rural residents who previously resided in an urban area for 10 years or more had a greater risk of lung cancer, independent of the smoking history than the corresponding rural residents who had no urban exposure.

In a recent report based on epidemiological findings, Stocks[246] hypothesized that air pollution accelerates the final stages of cancer growth in susceptible persons who have reached an advanced point in the latent interval of the disease.

Attempts have been made to correlate the amount of atmospheric BaP pollution with the development of lung cancer. Stocks and Campbell[248] observed a higher incidence of lung cancer among persons living in an area in which BaP was known to be present in the atmosphere. Shahab,[221,222] Stocks,[244,245] and Gorman [83] observed a relationship between the increased mortality from lung cancer and the concentration of carcinogenic PAH in urban areas.

In contrast, Sawicki et al.[188,217] in several studies have not been able to demonstrate a correlation between lung cancer death rates and the amount of atmospheric BaP. Sawicki[188] suggests that because airborne carcinogens are so numerous, many have not yet been identified. He further states, "The number and type of carcinogens found in the atmosphere indicate that attempts to correlate carcinogenicity of the mixtures in our chemical environment with concentrations of BaP are probably naive in most cases and spring from our lack of knowledge of the composition of the mixtures with which we are dealing." Hueper et al.[109] were unable to find a correlation in a combined analytical and experimental bioassay study using samples of polluted air from eight metropolitan centers in the United States.

It is now generally accepted that usually many factors are involved in the initiation and promotion of cancer. Consequently, a correlation between the incidence of cancer and any single suspected environmental factor is extremely difficult to establish as well as quite limited in usefulness.

2.1.1 Particulate Matter

The occurrence of gastric cancer has been linked with the presence of suspended particulate matter in the atmosphere. Anderson and Coffey[7] hypothesized that the causative agent of gastric cancer is associated with soot. Winkelstein and Kantor[43] have found that mortality rates from gastric cancer in a selected population were twice as high in areas of high suspended particulate air pollution as in areas of low pollution in a northeastern United States industrial area. The exact nature of the particulate was not specified; however, in areas of high industrial air pollution, soot is usually a significant constituent. In a Nashville study,[295,296] soiling indices were found to correlate directly with mortality from stomach cancer and with prevalence of bladder, esophagus, and prostate cancers. No clear correlation was found between soiling indices and mortality from lung, bronchial, or large intestinal cancer.

In 1963, Litvinov et al.[144] studied the relationship between pulmonary cancer in man and air pollution resulting from the discharge of carcinogens by aluminum plants. Over 10 kg of BaP were discharged into the air daily resulting in the deposit of an average of 9.1 μg per square mile per day of this material on the ground in the area of the plant. These high concentrations of BaP were implicated as a cause of chronic morbidity of the respiratory tract.

Konstantinova and Chertova[117] studied the effect of dust and other airborne contaminants on lung cancer morbidity. Two population districts of Ufa in Russia were studied. The first area was located between two petroleum refineries and the other was situated 20 kilometers from the refineries. The symptoms characteristic of chronic hydrocarbon poisoning were observed more than three times as often in the population near the refineries than in the one 20 kilometers away. The lung cancer mortality rates per 10,000 population were 0.8 for the noncontaminated area and 1.28 for the contaminated area.

The carcinogenic properties of soot are believed to result from the presence of certain adsorbed PAH.[248,271] Kotin and Falk[120] have studied the role of soot in lung cancer. Their findings indicate that soot is a powerful carcinogenic agent because of its ability to adsorb large quantities of known carcinogens. In addition, certain physical properties of the soot, such as particle size, facilitate transport into the lungs and elution of these carcinogens by body fluids.

2.1.2 Particle Size

PAH and other organic carcinogens are primarily present in the atmosphere as adsorbed compounds on soot particles.[119] The biological effect of the organic carcinogens is critically related to the physical properties of the particle on which it is adsorbed. Particle size largely determines the extent to which particles can penetrate the tracheobronchial tree.[120] Particles in the size range of 125 Å to 2.5 μ are of great biological importance. Particles larger than 2.5 μ gaining host entry are largely retained in the mucous membranes of the nose, oral cavity, pharynx, and nasal sinuses. Particles less than 125 Å remain largely suspended in the circulated air, and thus pulmonary retention of these particles is rather small. The pulmonary retention of particulate matter by the lung in relation to particle size has been given by Dautrebande et al.[47] Figure 1 shows the relationship between retention of particulate matter and particle size.

The size of the particulates on which the carcinogenic hydrocarbons are adsorbed also determines the rate and elution of the hydrocarbons from the particles.[70] Steiner,[236] using commercial carbon blacks, was able to relate the skin carcinogenic activity of adsorbed carcinogens to the size of the soot particle and to the presence of natural eluting substances in

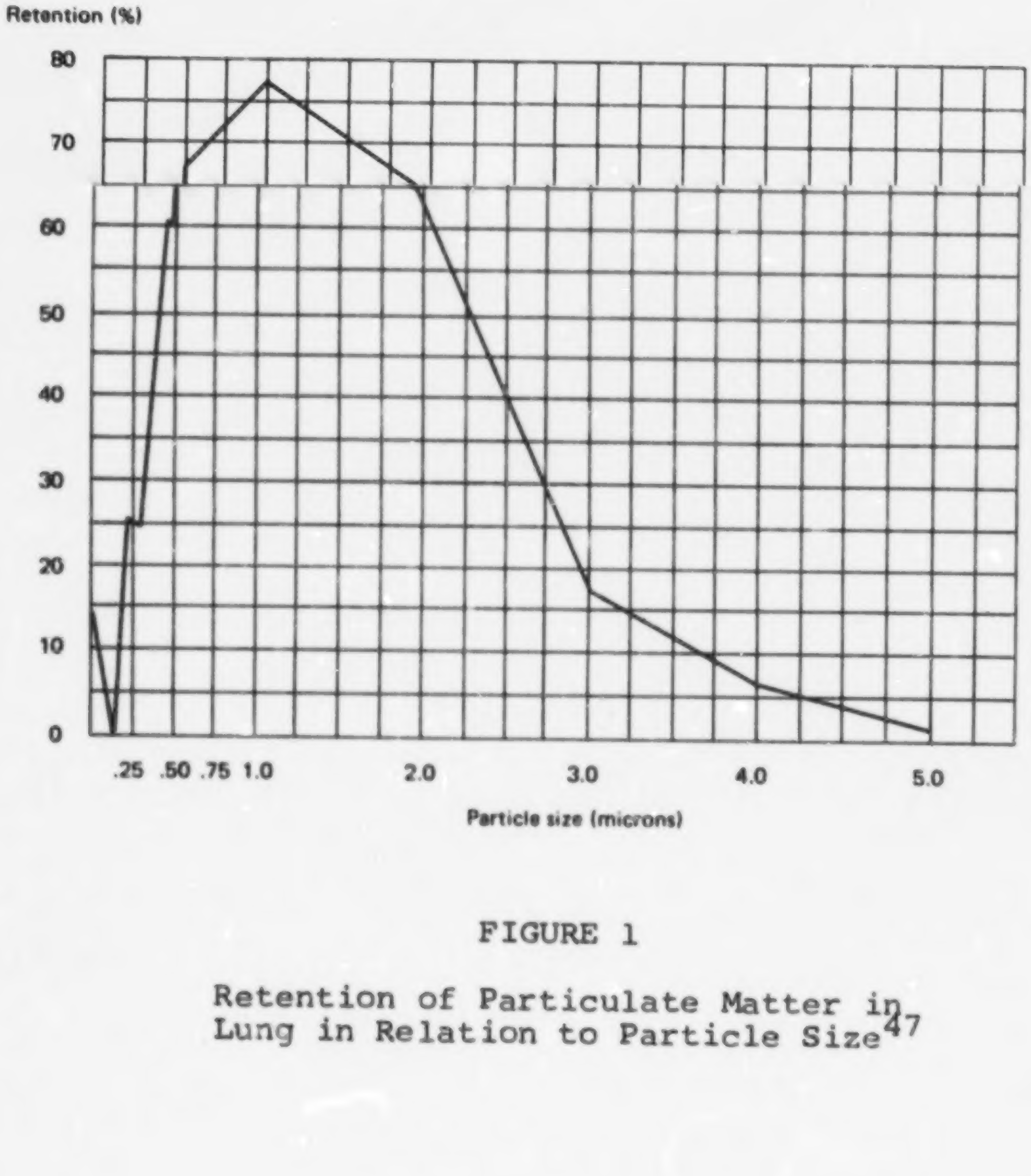

FIGURE 1

Retention of Particulate Matter in Lung in Relation to Particle Size[47] the skin at the point of deposition. He concluded, "The principles of natural and conditioned carcinogens, of solvent elution, and of adsorption are advanced to explain some clinical and epidemiological observations on human skin and lung cancers, and on the role of preceding pathological lesions in predisposing to pulmonary tumors." It has been suggested that the solvent action of lipids and sebaceous secretions on the skin exerts an eluting effect by liberating the carcinogenic PAH from the soot particle.

In chemical studies of soot recovered from human lungs during autopsy, Falk _et al_.[70] could not demonstrate the presence of BaP, although traces of pyrene were detected. It was possible, however, to demonstrate experimentally the entry of soot particles of appropriate size into the cells of the respiratory tract of mice, rats, and rabbits, both by histological studies and by the fluorescence of BaP (using fluorescence microscopy techniques).[120] It then became necessary to determine the effect of cellular and plasma proteins on the elution of PAH from soot. It was found that PAH is readily eluted from commercially prepared soot particles of 0.5 microns. When the particle size population was mixed, the liberated PAH from the larger particles was adsorbed by the smaller particles. Thus, particles of less than 800 Å in diameter do not yield PAH in the presence of physiological eluting agents. Instead, they serve as scavengers for the readsorption of the PAH eluted from larger particles.

2.1.3 Irritants

In addition to the normally recognized carcinogens, other organic compounds usually present in polluted urban air may act as irritants to the respiratory system, triggering physiological responses. These responses may result in the formation of malignant tumors or render the system more susceptible to the usual pathogenic effects of substances generally recognized as carcinogens. Irritants in the respiratory environment can interfere with ciliary activity and the flow of the mucous stream in such a way that particulate matter accumulates on the underlying cells. The typical response of ciliated mucous-secreting epithelium to irritant aerosols is characterized by a small increase in the rate of flow, followed by a slower flow rate that eventually returns to normal. The biological effect of the alterations in the rate of mucous flow is one of increased particle retention, enhancing the opportunity for tumor formation. This phenomenon represents a step in the pathogenetic sequence in which compounds that are not in themselves carcinogenic appear to facilitate the biological activity of compounds capable of inducing cancer in the respiratory tract.[119]

Among the compounds normally present in polluted urban air implicated as irritants are: formaldehyde, acetaldehyde, acrolein, propionaldehyde, formic acid, acetyl peroxide, peracetic acid, propylene oxide, and cyclohexene oxide.[68]

2.1.4 Studies with Biological Material

Cultures of human fetal lung tissue were exposed to BaP by Lasnitzki,[41] and to fractions of cigarette smoke condensate by Lasnitzki and Kennaway[136] and by Lasnitzki alone.[135] Basal cell hyperplasia and metaplasia of the epithelium, proliferation of bronchial units, and suppression of mesenchymal elements occurred during 2 or more weeks of cultivation under continuous exposure to BaP. A hydrocarbon-free fraction of cigarette smoke condensate was also active (producing squamous metaplasia), indicating that the effects of the condensate could not be attributed to hydrocarbons alone.

Rounds *et al.*[179] demonstrated that an established line of human conjunctival cells show an increased growth rate and undergo increased chromosomal aberrations when treated with chloroform extracts of automobile exhaust. He also showed that 3-methyl-4-dimethyl-amino-azobenzene induced the following changes in human conjunctival cells in a suitable growth medium: growth stimulation, increased chromosomal stickiness and scattering during mitosis, and a decrease in a positive staining reaction for phospholipids.[178]

Allison and Mallucci[6] demonstrated that the carcinogens BaP and 9,10-dimethyl-1,2-benzanthracene (DMBA) are concentrated by the lysosomes. The genetic perpetuation of carcinogen-induced metabolic changes has been explained on the basis of specific disruptions in metabolic regulatory circuits.[163] Experiments which purported to show an intercalation (mutagenic interaction) between carcinogens and deoxyribonucleic acid (DNA) have been criticized by Giovanella.[78]

Hsu _et al_.[106] described the inhibitory effect of certain carcinogenic aromatic hydrocarbons on the replication of single stranded ribonucleic acid (RNA) and DNA. Hsu _et al_.[107] later demonstrated the inhibition of viral nucleic acid and protein synthesis in _Escherichia coli_ by DMBA.

2.2 Effects on Animals

2.2.1 Commercial and Domestic Animals

No information is available concerning the effects of organic carcinogens on commercial and domestic animals. However, Pybus[165] reports that virtually every form of benign or malignant tumor has been found among domestic animals. Cancers of the mouth, throat, breast, and other body parts are relatively common among older cats and dogs.

Stewart[240] examined 36 wild mammals and birds from the Philadelphia Zoo for pulmonary cancer, pulmonary adenomatosis, and squamous metaplasia. Histologic material available on 31 of the animals indicated: adenocarcinomas in 11 birds of the family Anatidae, a silver pheasant, a red jungle fowl, and a coypu; squamous cell carcinoma in a North American otter; undifferentiated small-cell carcinoma in a Java sparrow; alveologenic carcinoma in a striped skunk; pleural mesotheliomas in a Cape hunting dog and a clouded leopard; adenomatosis, squamous metaplasia, or both in a red fox, puma, North American otter (which also had squamous cell carcinoma of the lung), squirrel monkey, peafowl, African eared vulture, Chinese myna, 2 toucan barbets, and a rabbit-eared bandicoot; tuberculosis in a civet; pneumonia in a kangaroo; and metastatic renal carcinoma of the lung in a red wolf.

2.2.2 Experimental Animals

The direct effect on animals of organic carcinogens, normally present in polluted urban air, is difficult to evaluate. Most of the information available on the effect of organic carcinogens on animals has been obtained under experimental conditions, which are different from the conditions which normally constitute the natural environment of the animal.

There has been extensive investigation of the effects on experimental animals of specific compounds that pollute the atmosphere. Much of the work has utilized skin painting with extracts of chimney soots,[27] road dusts,[28] and vehicular exhausts,[104,124] or injections of these extracts.[109,125,140,141] In general, inhalation studies have not attained the same degree of success as those using painting and injection techniques. The induction of bronchogenic carcinomas in experimental animals has often required such drastic treatments as transfixion of the lungs with carcinogen-impregnated threads,[130] intrabronchial implantation of wire pellets impregnated with carcinogens,[130] and the use of radioactive materials.[134]

In recent years, successful production of experimental lung cancer has been reported through use of the following test compounds or mixtures: "artificial smog" (ozone-treated gasoline vapor),[125,170] BaP adsorbed on hematite,[182,183] BaP in polysorbate 80,[155] an aerosol containing both ozonized-gasoline and influenza virus,[123,281] and mixtures of phenolic and nonphenolic extracts of coal tars.[263] The investigations of Kotin and his co-workers,[123,125,281] and of Tye and Stemmer,[263] employed natural inhalation of the "polluted air," whereas the other experiments used intratracheal instillation.

For test animals, investigators have often used a strain of rodents that is genetically susceptible to "spontaneous" formation of the type or types of cancer being studied.

The carcinogenicity of 14 mono-, di-, and trimethylated BaP was studied by Lacassagne et al.[133] using laboratory mice as test animals (three injections of 600 μg each). The majority of these compounds showed highly pronounced sarcomagenic properties, both regarding the percentage (almost 100 percent) of animals developing tumors and the latency period (100-150 days). Many of these homologues were more active than nonsubstituted BaP. From this study, the authors concluded that introduction of more than three methyl groups into the BaP molecule would lead to a loss of carcinogenicity.

Stokinger and Coffin[250] have discussed the importance of the enhancement of organic carcinogen action (such as that of BaP) with seemingly inert particles. Iron oxide in particular appears to have properties that possibly contribute to cancer production. These authors cite the work of Saffiotti et al.,[180,181,184] who produced a variety of malignant tumors in the lungs of hamsters. The animals were intratracheally injected with a saline suspension of BaP ground together with hematite (Fe_2O_3)[a] as a carrier dust in amounts equivalent to 3,000 μg of each chemical (a very high dose). Fifteen weekly injections were given. Two important facts were revealed in this study: a high incidence[b] of lung cancer was produced, up to 100 percent of the animals in some experiments; and these lung cancers mimicked all the cell types seen in human lung cancers, i.e., squamous cell carcinoma, anaplastic carcinoma, adenocarcinoma, and even tracheal cancers. Dose-response effects were indicated, as was the possibility that a single high dose could induce cancers in the system. According to Saffiotti _et al._[181] the increased carcinogenic action is due to the iron oxide, which penetrates the bronchial and alveolar walls into the lung tissue without extensive damage or destruction of the ciliary and mucous barrier; the iron oxide also acts as a vehicle to transport the carcinogen to the lung tissues. The carcinogen is then eluted from the particulates and spreads diffusely throughout the tissue. They surmise that the rate of removal of BaP from the respiratory tract is slowed by action of the inert dust as it is stored in macrophages. Thus, the carcinogen remains in the lung, unmetabolized in high local concentrations—an important factor in producing cancer with BaP. They also suggest that such a mechanism is a realistic concept of what actually occurs in nature as man breathes the polluted air—i.e., carcinogens adsorb on iron oxide or other "inert" particles which act as a vehicle to transport the carcinogens into the lungs through the respiratory tract lining to the lung tissues, where the carcinogens are eluted by the cell plasma. However, it is yet to be shown that BaP is adsorbed onto iron oxide particles in the atmosphere.

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[a] Iron oxide was chosen as the carrier dust because it has no extremely irritating or toxic effects. Saffiotti believes that in order to carry the carcinogen in high concentrations to healthy cells, an inert carrier is required--that is, a carrier which does not destroy the cells.

[b] Benzo(a)pyrene alone has induced cancer in the lungs of experimental animals, but usually with some difficulty and in low yield.

Rigdon and Neal[172] studied the absorption and excretion of BaP using ducks, chickens, mice, and dogs as test animals. There was no apparent acute injury when large amounts (e.g., 250,000 μg for ducks) of BaP crystals and/or BaP suspended in a physiologic solution of sodium chloride, with a 1 percent solution of polysorbate 80 were given orally to ducks, chickens, mice, and dogs and intratracheally to ducks. BaP was detected in the blood of ducks as well as in the blood and bile of chickens and dogs. The presence of BaP was also detected in the skin of the chickens and mice. The mesenteric tissue, the gallbladder and kidneys, and the urine of the treated mice, as well as the kidneys of treated chickens and ducks contained BaP.

Rigdon and Neal[173] found that although white Swiss mice (59 or more per group) fed commercial laboratory pellets of BaP rarely had spontaneously occurring tumors in the stomach, they did have spontaneously occurring pulmonary adenomas. BaP crystals were added to the commercial ration in concentrations of 250 and 1,000 µg per gram of food and fed routinely to the mice. Papillomas and squamous cell carcinomas in the first portion of the stomach as well as an increase in the number of pulmonary adenomas resulted. All the mice fed the 1,000 µg BaP-containing ration for 86 days or longer developed gastric neoplasms. When mice born of mothers fed BaP during pregnancy and lactation were fed the control ration after weaning, gastric tumors did not develop; however, littermates fed BaP did develop such tumors.

These same investigators[154] studied the growth of young mice fed BaP. They found that the rate of increase in weight of litters of young mice nursed by mothers fed BaP was lower than that of litters from lactating mothers fed a normal ration. In some mice in the BaP-fed litter there was a decrease in weight that began at 10 to 12 days of age. After the young mice were weaned and fed a standard ration, their weight still remained lower than normal. This diminution in weight was attributed to a decrease in nutrition and not to a toxic effect resulting from the BaP.

Toth and Shubik[261] investigated carcinogenesis in AKR mice injected subcutaneously with BaP and dimethylnitrosoamine (DMN). In contrast to controls, mice injected with BaP produced malignant lymphomas more rapidly; and they developed lung adenomas. The DMN had no apparent effect on the development of virally mediated lymphomas, but did cause both benign and malignant liver tumors and lung adenomas.

Pylev[166] investigated the effect of the dispersion of soot on the deposition of BaP in the lung tissues of rats. Two contrasting kinds of carbon black (soot) were administered intratracheally: 5,000 μg channel black, with particles of 0.01 μ; and 5,000 μg thermal decomposition black, with particles of 0.3 μ. He found that the coarsely dispersed decomposition black promoted rapid disappearance of BaP from lung tissue, whereas the finely dispersed channel black impeded the elimination of BaP and facilitated its decomposition.

Shahab *et al.*[225] studied the importance of local retention of carcinogenic agents in the pathogenesis of lung cancer in rats. In this experiment 280 animals were given 5,000 μg BaP in suspensions of india ink in three doses by intratracheal intubation. It was found that BaP retention was a function of the number of administrations of BaP, as the number of exposures to BaP increased, the retention in the lung was found to increase.

Tomingas[260] found that the subcutaneous implantation of starch-encapsulated soot on the back of rats resulted in the formation of sarcoma in low yield. Herrold and Dunham[99] showed that repeated intratracheal instillations of BaP suspended in polyoxyethylene sorbitan monostearate (Tween 60) induced papillomas and carcinomas of the trachea, main-stem bronchi, and bronchioles in Syrian hamsters. The mucosa of the tracheobronchial tree showed both regenerative and atypical epithelial changes. Neoplastic lesions were not induced in another group of animals that received intratracheal instillations of BaP dissolved in olive oil. Shubik[227] reported that bronchogenic carcinoma could be induced in hamsters by using a colloidal suspension of 7,12-dimethylbenz(a)anthracene administered by endotracheal intubation, but found that repetition of the study with BaP yielded uniformly negative results.

Herrold[98] studied the effects of BaP, cigarette smoke condensate, and atmospheric pollutants on the respiratory system of Syrian hamsters. He observed that benign and malignant tumors of the trachea, bronchi, and bronchioles were induced following intratracheal instillation of BaP suspended in Tween 60. Only atypical epithelial changes suggestive of precancerous lesions were observed with BaP suspended in distilled water. No significant changes were noted in the animals that received intratracheal instillation of BaP dissolved in olive oil. These findings suggest that the vehicle for the carcinogen as well as the physical state of the carcinogen are important factors in carcinogenesis.

The intratracheal instillation of cigarette smoke condensate and atmospheric pollutants in the hamsters produced regenerative epithelial changes of the tracheobronchial mucosa. These lesions included basal cell hyperplasia and peribronchial and peribronchiolar proliferation. Atmospheric pollutants induced extensive adenomatous proliferation involving large areas of the lung in all of the test animals. No tumors of the respiratory tract were induced either with cigarette smoke condensate or atmospheric pollutants.

Bogacz and Koprowski[17] investigated the comparative carcinogenic properties of air pollutants, tobacco tar, and BaP by means of correlated cytopathologic studies, utilizing the uterine cervix of mice as a target organ. It was demonstrated that mice of the ZBG and C3H strains treated intravaginally with air pollutants and tobacco tar developed cellular abnormalities and histologic lesions that were morphologically indistinguishable from those accompanying the development of BaP-induced carcinoma.

The carcinogenicity of atmospheric pollutants in mice has been demonstrated with organic extracts collected from various sources, using various techniques (Table 4 in the Appendix). When pollutant extracts are administered to mice, whether by painting or by subcutaneous injection, local tumors, papillomas, carcinomas, or sarcomas—sometimes accompanied by multiple pulmonary adenomas—have generally resulted. Notable exceptions were: (1) the high incidence of distant tumors, hepatomas, and lymphomas, in addition to multiple pulmonary adenomas; and (2) the virtual absence of local tumors following subcutaneous injection of relatively small concentrations of organic pollutant extracts in infant mice (Table 4 and 5 in the Appendix).[64]

Saffiotti _et al_.[183] reported that vitamin A prevented development of tumors in hamsters. Syrian golden hamsters of both sexes received 10 intratracheal instillations each of BaP and hematite suspended in saline. One group received no further treatment and developed 13 squamous tumors and 13 cases of squamous metaplasia in 53 exposed animals. One week after the end of the BaP treatment, the second group began receiving stomach tube feeding of vitamin A palmitate twice weekly (continued for life). In this group of 46 animals, only one developed a microscopic squamous tumor in the bronchus, while another developed a patch of squamous metaplasia in the trachea. The incidence of forestomach papillomas was also reduced markedly by vitamin A treatment. The authors suggested that vitamin A has a systemic inhibitory effect on the induction of squamous changes (metaplasia as well as benign and malignant squamous tumors) in the columnar mucous epithelium of the respiratory tract.

In studying the influence of phenols in the production of carcinomas, Tye and Stemmer[263] exposed five groups of mice (20 per group) to aerosols containing blends (120 μg/liter) of coal tar extracts, including phenols. The mice were exposed 2 hours, three times weekly, for 55 weeks. Animals were sacrificed at various intervals. The lungs and tracheas of all mice were then examined grossly and microscopically for neoplasms or relevant morphologic changes. After 46 weeks, among 32 survivors in two groups, which received similar aerosols containing phenols, there were 4 cases of adenocarcinoma, 19 of intrabronchial adenoma, and 10 of squamous metaplasia. In

20 survivors of another group, which received the same tar without phenols, there was no incidence of adenocarcinoma; 11 had intrabronchial adenoma and 2 had squamous metaplasia.

Gardner[77] reported that laboratory mice exposed to community photochemical smog levels for a 16-month period showed a slight but statistically insignificant increase in lung tumor development (adenoma) in the aging animals, when compared with control animals that were exposed to filtered air.[77]

2.2.2.1 Effects on Animal Tissue

Lasnitzki[41] studied the effect of the carcinogenic hydrocarbons 9,10-dimethyl-1,2-benzanthracene (DMBA), BaP, and methylcholanthrene (MC) on organ cultures of suckling rat trachea. It was found that these hydrocarbons caused loss of differentiated tracheal epithelial cells and of mesenchymal elements (including chondrocytes), but not of basal cells. The mitotic rate and the proportion of cells incorporating H^3-thymidine increased in response to hydrocarbons, but the increase in H^3-thymidine uptake and mitotic rates was not always proportionate, nor were these responses alike for all hydrocarbons.

The effects of DMBA, BaP, and MC were similar in that all produced clear-cut increases in the proportion of basal cells undergoing DNA synthesis.

In studying the effect of MC on prostate glands of mature mice, Lasnitzki[41] observed that hyperplasia resulted during exposure to 2 μg/ml and 4 μg/ml for 10 days; this process continued after withdrawal and was accompanied by squamous metaplasia. Mitosis was increased 4 days after exposure to MC.

Mitosis and DNA synthesis in mouse prostate gland tissue were compared by Lasnitzki and Pelc.[137] They concluded that mitosis was stimulated before DNA synthesis.

2.3 Effects on Plants

No information on the effects of organic carcinogens on plants has been found in the literature.

2.4 Effects on Materials

No information has been found indicating that materials of commercial or industrial importance are affected by organic carcinogens.

2.5 Environmental Air Standards

Recommended limits of 200 μg/m^3 for an 8-hour workday have been adopted by the American Conference of Governmental Industrial Hygienists[258] for coal tar pitch volatiles (benzene fractions containing anthracene, BaP, phenanthrene, acridine, chrysene, pyrene, etc.).

3. SOURCES

3.1 Natural Occurrence

Organic carcinogens are primarily unwanted by-products of imperfect combustion. However, a few sources of organic carcinogens might be defined as naturally occurring.

Bituminous coal contains BaP, benz(a)anthracene, and other PAH.[264] However, studies in England reveal a lower incidence of lung cancer among coal miners than in the population at large.[80,115] Consequently, although carcinogenic agents are present in raw coal, they have no apparent biological effect in that form.[264]

Asbestos miners, in comparison to coal miners, have a greater potential for developing malignancy.[94] Two of the three types of asbestos used industrially contain appreciable quantities of natural oils. These oils, which adhere to asbestos particles, contain BaP.[93] The quantities (1 to 5 μg/100 g asbestos) are small enough that their presence may play no more than a minor carcinogenic role.[94]

Another potential naturally derived source of airborne carcinogens has been reported by Troll,[262] namely, various molds in the environment that possibly produce toxic compounds, some of which may be carcinogenic.

3.2 Production Sources

Prior to the introduction of gasoline and diesel engines, PAH were emitted primarily from the burning of coal and other solid fuels used for home and industrial heating as well as for the production of industrial products and power. However, in recent times the use of gasoline and diesel engine fuels has resulted in a new major source of PAH.

The U.S. Public Health Service, recognizing the need for specific emission data, has obtained information concerning those sources that involve burning conventional fuels and certain commercial and municipal solid wastes.[90,91] The sources of heat generation that were tested ranged in size from residential heaters to heavy industrial power plant boilers and employed the following firing methods: (1) pulverized coal burners, chain grate stokers, spreader stokers, underfeed stokers, and hand-stoked coal burners; (2) steam-atomized, centrifugal-atomized, and vaporized-oil burners; and (3) premix gas burners. The incineration sources tested ranged from small commercial incinerators to large municipal incinerators. Open-burning sources and several industrial processes were also tested. From these studies, in conjunction with the annual consumption and production figures, sufficient emission data were collected to reveal the probable major sources of carcinogenic agents as indicated in Table 6, in the Appendix. In interpreting the significance of this information, it should be remembered that the calculation of total emissions involved a considerable amount of estimation, as well as a number of assumptions, with respect to both emission rates and annual consumption or production figures. Also, the aggregate emissions from a number of small sources not considered in this study, although probably small, cannot be estimated.[91]

As shown in Table 6 in the Appendix, the sources were separated into four major categories: heat generation, refuse burning, industrial processes, and motor vehicle operation. This study revealed that each category contributes to the atmospheric loading of BaP. Generally, the importance of a particular category or source has been evaluated in terms of the United States as a whole, but the importance of a particular source, relative to concentrations found in the atmosphere, undoubtedly varies considerably with locality; e.g., although no coal is burned in Los Angeles County, the city of Los Angeles has areas of exceptionally high traffic density. Other factors may also influence the concentrations of BaP and other polynuclear hydrocarbons found in the atmosphere, such as decomposition or reaction with smog constituents in the atmosphere.

The results and implications from these studies have been summarized by Hangebrauck et al.[91] as follows:

(1) Although each process surveyed undoubtedly contributes to the amount of BaP in the atmosphere, the most important source of BaP is the inefficient combustion of coal, typified by residential and small industrial coal-fired furnaces.

(2) The efficient combustion of coal in modern industrial-process heating boilers and power plants and the combustion of fuel oil and natural gas do not appear to be significant contributors.

(3) In refuse burning, as in coal burning, efficiency of combustion governs the emission of polynuclear compounds. Inefficient combustion in small incinerators as well as open burning results in considerable formation of BaP and other polynuclear hydrocarbons, whereas efficient combustion in municipal incinerators results in very little BaP formation.

(4) Results from direct and indirect sampling of industrial sources, although not conclusive, indicate that the following processes are not major sources of BaP: an asphalt air-blowing process (pyrene emissions were high), an asphalt hot-road-mix plant, a carbon-black manufacturing area, a steel and coke manufacturing area, and a chemical industry complex.

(5) Direct samples of the effluent from the catalyst regenerators of petroleum catalytic cracking units indicate that Houdriflow and Thermofor (air lift) units can be significant industrial sources of BaP and other polynuclear hydrocarbons. Emission of these compounds can be, and frequently is, reduced to negligible amounts through the use of CO-waste heat boilers on individual "cat-cracker" catalyst regenerators. Thermofor (bucket lift) and Fluid units incorporate catalyst regenerator designs that result in minor emissions only. Considerable additional testing would be necessary to statistically assure the evaluation of contributions from catalyst regenerators, as for all of the sources tested.

(6) Consideration of the emission rates determined for gasoline-powered automobiles and trucks, as well as of their annual fuel usage, indicates that motor vehicles are a major contributor of BaP in the atmosphere. This is confirmed by Colucci and Bregeman,[39] who report automotive BaP contributions of 5 to 42 percent, based on ratios of lead to BaP in exhaust and in the atmosphere. Evidence indicates that old high-mileage vehicles and those with poorly adjusted engines have the highest emission rates.

(7) Limited data indicate higher emission rates for gasoline-powered trucks than for automobiles. Diesel-powered

trucks may also have higher rates;[251] however, diesel fuel usage by trucks and buses accounts for only about 4 percent of the total petroleum consumption for motor vehicles. The overall contribution from all trucks and buses, both gasoline and diesel-powered, possibly exceeds that from automobiles, although the total fuel usage for this category is about half that for automobiles.

See Section 3.3 for further discussion of PAH emissions from automotive exhaust.

A number of studies which deal with PAH emission from specific types of industries have been reported and are discussed briefly in the following paragraphs.

The PAH composition of air polluted by coal-tar pitch has been studied by Sawicki et al.[211] Coal-tar pitch pollution is characterized by much higher ratios of pyrene to BaP, BaP to benzo(g,h,i)perylene, and BaP to coronene, when compared with other types of pollution. Sawicki[213] also suggested that these ratios are also probably characteristic of the two types of pollution produced from the combustion of gasoline and coal.

Specific studies have been made of BaP levels in an iron and steel works,[254] of PAH concentrations both in a gas works retort house[139] and in stack gases from pulp mills,[96] and of BaP in coke oven wastes[292] as well as in the vicinity of a coal briquet factory.[116] The atmospheric emissions produced by oil burners has been reported to be 0.04 to 0.10 pounds of BaP per million pounds of oil.[231] Methods for sampling from various coal-fired steam-generating installations are also reported.[54] A Russian study states that the asphalt, concrete, tar roofing, and rubber industries are carcinogenic foci with regard to pollution of city air.[45]

No detailed studies of the distribution of pollutants by prevailing winds have been reported.[91,270] However, it can be inferred that after distribution by the winds, the carcinogens fall back to earth. If the carcinogens fall into water, they may spread for considerable distances. Il'nitskii and Varshavskaya[111] in a review article have discussed PAH determinations in ground water, streams, and harbors. PAH were also detected in the aquatic life of these waters.

3.3 Product Sources

As discussed earlier, exhaust from internal combustion engines has resulted in a significant new source of PAH. The emission rate per gallon of fuel and the annual emission of BaP are presented in Table 6 in the Appendix.

Carcinogenic emissions from automotive sources can be divided into at least two major categories: PAH, and the photochemical pollutants that are precursors of alkylating agents. For PAH emissions, Kotin and Falk[119] have reviewed the literature pertaining to analysis of exhaust prior to approximately 1963. The primary conclusions are that a broad spectrum of PAH, including several carcinogens, can be detected in exhaust products; and the yield of PAH decreases with the efficiency of the engine used. In regard to the latter conclusion, Hoffmann and Wynder[104] have quantified the BaP yield on the basis of engine mileage and found that the BaP concentration varied from 5 μg/minute sample early in engine life (8,000-12,000 miles) to 27 μg/minute late in engine life (29,000-33,000 miles). When the diesel exhaust from an engine operating inefficiently under maximum load at varying rpm's was analyzed, BaP yield was found to vary from 876 μg/minute to 1,687 μg/minute.

More recent studies on automotive exhaust products have been conducted in the following areas: (1) production of PAH by cars and trucks, (2) contribution of automotive PAH to total PAH, (3) carcinogenicity of automotive exhaust, and (4) formation of carcinogens other than PAH. Each of these areas is discussed below in greater detail.

The reports[19,79,89,104] dealing with the production of PAH have fairly uniform conclusions. For example:

(1) Automobiles with properly adjusted carburetors generated and discharged less carbon monoxide and less BaP into the atmosphere.

(2) The highest concentrations of BaP and carbon monoxide were discharged in exhaust gases from automobiles operated at low rpm, usually at the time of starting or accelerating. Aldehyde emissions showed a similar pattern.[159]

(3) The concentrations of BaP and carbon monoxide pollution in atmospheric air can be reduced substantially by controlling carburetor operation at all times, particularly when starting and moving into line with the traffic; keeping the carburetor clean and well adjusted; and reducing the number of stops and starts at crossings and light signals to a minimum. This can be accomplished with proper regulation of traffic, as for example through better synchronized signal lights and use of overhead and underground auto routes which would allow automobiles to travel without making many stops.

Several studies relating the contribution of automotive PAH to total PAH have been reported. A recent test was conducted in Detroit, Mich.[39] The study showed that the mean contributions by automobiles to the total amount of BaP in the air at three sites were: 18 percent for freeway, 5 percent for downtown, and 42 percent for suburbs (in winter).

These results are based on the dilution factor of exhaust concentration over atmospheric concentration found for lead. Based on the carbon monoxide dilution factor, the results were: 35 percent for freeway, 10 percent for downtown, and 32 percent for suburban areas (in winter). An earlier study from the same laboratory had estimated the PAH concentrations to be lower.[21]

The carcinogenicity of automotive exhaust has also been studied.[84,105,286] Wynder and Hoffmann reviewed the pertinent literature prior to about 1962.[286] There is general agreement that exhaust tars are carcinogenic to experimental animals, the major portion of the activity is due to PAH, and the emissions are dependent upon the type of fuel used.

Another source of PAH is cigarette smoking. (The relation of cigarette smoking to cancer is briefly discussed in Section 2.)

Photochemically reactive compounds, which may be precursors of carcinogenic alkylating agents, are emitted as by-products of incomplete combustion. The major sources of these pollutants are automobile operation and use of natural fuels

The foregoing discussion outlines the major product sources of carcinogens. There are other reports in the literature of possible sources of carcinogens. The Weisburgers[275] have reported that nitrosamines are included in 20 patented products. Rubber tire dust is also given as a source of BaP.[69] There are also several reports concerning petroleum products which contain carcinogens.[229,265,290]

3.4 Environmental Air Concentrations

In a survey of 103 urban and 28 nonurban areas of the United States in the late 1950's, the U.S. Public Health Service found that concentrations of PAH were present in the atmosphere of all locations studied.[213,217] Selected values for the winter months (January through March) of 1959 are given in Table 7 in the Appendix.[119,217] These values show the striking contrast in urban and rural BaP concentrations. Additional recent studies in the United States[109,127,214] and other countries [29,30,150,223,272] have shown a similar wide distribution and urban-rural differences. The concentration of nine various other PAH in particulate matter of selected cities was measured in 1958-1959 (see Table 8, in the Appendix).[213] The data indicate that BaP is only a small percentage of the PAH, ranging from approximately 5 to 20 percent of the nine PAH measured.

There is also a wide seasonal variation in BaP concentrations in urban areas. Data showing this variation are given in Table 9 in the Appendix.[39,90,103] These data are relatively outdated, yet they have been presented in recent surveys by Hoffmann and Wynder[103] and by Sawicki.[188] Similar surveys have been conducted in Australia,[35] Belgium,[176] Canada,[150] Czechoslovakia,[76,230] Denmark,[29] Germany,[100,131] Great Britain,[30,249,271-273] Hungary,[185] Italy,[18,161,266,267,293] the Netherlands,[58] Norway,[30] Poland,[114] South Africa,[146] and Sweden.[73]

Concentrations of BaP in 106 urban and nonurban areas of the United States were measured by the National Air Sampling Network in 1966.[4] These data are tabulated in Table 10 in the Appendix. The maximum station average value reported was 0.0112 μg/m³ for urban areas and 0.00145 μg/m³ for nonurban areas; the arithmetic average value was 0.00279 μg/m³ and 0.00035 μg/m³, respectively.

4. ABATEMENT

Emissions of PAH are generally associated with conditions of incomplete combustion of carbonaceous materials. Emission sources include motor vehicles, refuse burners, and domestic and industrial facilities that burn coal, oil, or gas. Methods presently being studied to control these emissions include more efficient techniques for combustion of fuels, collection or trapping of emissions (particularly in the form of particulates), and use of combustion treatment techniques for the emissions (such as direct-flame or catalytic afterburners). In a 1967 study of polynuclear hydrocarbon sources, Hangebrauck et al.[91] made the following comments on abatement for particular sources:

(1) Heat generation. Replacement of inefficient coal-fired furnaces would greatly reduce emissions attributable to heat generation.

(2) Motor vehicles. Control systems applied to automobiles and trucks for the purpose of reducing emissions of total gaseous hydrocarbons should reduce emissions of BaP and other polynuclear hydrocarbons, but no data are available to prove that this is possible.

(3) Refuse burning. The burning of all refuse (especially that with a high ratio of hydrogen to carbon) in

modern municipal incinerators or disposal by noncombustion methods would almost eliminate emissions attributable to refuse burning.

Hangebrauck *et al.*[91] found that emissions of polynuclear hydrocarbons from the catalytic regenerators of petroleum catalytic cracking units can be reduced to negligible amounts through the use of carbon monoxide-waste heater boilers. The data (see Table 6 in the Appendix) indicate well over 99 percent reduction upon passage through the carbon monoxide boiler.

In addition, fuels containing BaP and other carcinogens may be thermally pretreated before use to remove or destroy these carcinogens. Yanysheva *et al.*[292] reported success in removing BaP from fuel bricks by heat treatment. Heating the fuel bricks in an electric oven at 60°C for 2 hours and 15 minutes reduced the BaP content from an average of 0.07 percent BaP to 0.0000017 percent.

5. ECONOMICS

No information has been found on the economic costs of organic carcinogen air pollution. However, in 1967, Ridker[169] estimated the cost to the economy of diseases associated with air pollution, including cancer of the respiratory tract. Although this study does not indicate the relative contribution of organic carcinogens as compared with inorganic carcinogens, occupational hazards, smoking, etc., the study does demonstrate that cancer as a result of air pollution may result in significant economic losses. According to Ridker,[169] the costs of a disease may be classified according to four categories: (1) those due to premature death, (2) those associated with morbidity (i.e., burial), (3) those incurred for treatment, and (4) those incurred for prevention or avoidance.

For the first category, Ridker reports a model that estimates the loss of output due to premature death. While Ridker elaborates considerably on the assumptions (using 1958 as a base year), the mathematical model is as follows:

$$V_a = \sum_{n=a}^{\infty} \frac{P^n_{a_1} \cdot P^n_{a_2} \cdot P^n_{a_3} \cdot Y_n}{(1 + r)^{n - a}}$$

where

V_a	is the present value of the future earnings of an individual at age a;
$P^n_{a_1}$	is the probability that an individual at age a will live to age n;
$P^n_{a_2}$	is the probability that an individual at age a, living to age n, will be in the labor force at age n;
$P^n_{a_3}$	is the probability that an individual at age a, living and in the labor force at age n, will be employed at age n;
Y_n	is the earnings at age n; and
r	is the rate of interest.

The costs of premature death were calculated from statistical data for the labor force.

Burial costs have been similarly calculated. If death is postponed, society delays using resources for burial. The gain thereby obtained is the difference between the present cost of burial and the present value of the expected cost of future burial. This can be calculated from the following formula:

$$C_a = C_o \left[1 - \sum_{n=a}^{\infty} \left(\frac{P^n_a}{(1 + r)^{n - a}} \right) \right]$$

where

C_a is the present value of the net expected gain from delaying burial at age a;

C_o is the cost of burial;

P_a^n is the probability that an individual at age a will die at age n; and

r is the discount rate.

The costs of treatment and absenteeism were estimated from specific data derived from a variety of sources.

As indicated in Table 2, cancer of the respiratory system is the most costly of these diseases.

No information has been found on the economic costs of the abatement of organic carcinogen air pollution.

TABLE 2

RESOURCE COSTS PER YEAR OF DISEASES ASSOCIATED WITH AIR POLLUTION[169] (Millions of Dollars)[a]

Type of Cost	Costs Associated with Selected Diseases						
	Cancer of the Respiratory System	Chronic Bronchitis	Acute Bronchitis	Common Cold	Pneumonia	Emphysema	Asthma
Premature death	518	18	6	b	329	62	59
Premature burial	15	0.7	0.2	b	13	2	2
Treatment	35	89	b	200	73	b	138
Absenteeism	112	52	b	131	75	b	60
Total	680	159.7	6.2	331	490	64	259

[a] Using a discount rate of 5 percent.

[b] Not applicable.

6. METHODS OF ANALYSIS

Several publications have compared methods and provided an overview of the role of analytical chemistry in carcinogenesis studies.[177,187,215,262,276] The methods of analysis generally consist of the following sequence of steps: (1) sampling, (2) extraction, (3) separation, and (4) analysis.

6.1 Sampling Methods

Organic carcinogens are usually associated with particulates and thus are collected as "particulates." Sampling is often accomplished with a "high-volume" air sampler, the particulates (with which the relevant compounds are associated) being collected on a glass-fiber filter. Collection into a liquid (cyclohexane) absorbent has also been employed. The collection process may continue for many days, in order to obtain sufficient quantities of material. A technique which has proved satisfactory for collecting BaP from high-temperature gas streams is the use of a series of water bubblers and condensate traps immersed in an ice-water bath, followed by a high-efficiency filter.[238]

6.2 Extraction Methods

The organic carcinogens are generally removed from the particulates by solid-liquid extraction, although liquid-

liquid extraction, sublimation, and distillation (for coal-tar mixtures) have also been used.[187]

Solid-Liquid Extraction. Particulates are commonly extracted from the atmosphere with either benzene or cyclohexane.[187] Other solvents used include chloroform, acetone, isooctane, methanol, and dimethylformamide, as well as benzene mixtures of aliphatic hydrocarbons or methanol. The solvent-particulate mixtures can be stirred at a certain temperature or a Soxhlet extraction can be used.

Recent studies have been concerned with the efficiency of extraction. Stanley *et al.*[233] showed that in the analysis of equal weights of air particulates enriched with BaP, benz(c)acridine, and 7H-benz(de)anthracen-7-one, the percentages of these compounds extracted ranged from 50 to 100, 15 to 100, and 40 to 80, respectively. The solvents were cyclohexane, benzene, methylene chloride, and acetone.

In another study Dubois *et al.*[58] stated that benzene was of questionable value as an extracting agent for the initial preparation of an air sample. The larger amounts of material extracted by benzene, as compared with cyclohexane, lead to analytical interferences in the subsequent analyses. Aigina and Mints[2] found somewhat similar results in that the extinction of BaP fluorescence called for a controlled content of 1, 12-benzoperylene as an internal standard.

6.3 Separation

Techniques used for separating the different organic carcinogens include column chromatography, thin-layer chromatography, and gas chromatography.[187]

6.3.1 Column Chromatography

Column chromatography is the common method for separation of a complex mixture of PAH.

Column chromatography techniques are sufficiently advanced that predictions can be made with regard to adsorbability of hydrocarbons on alumina. Structural studies[187] have shown that adsorbability is greater for:

(1) A compound with more rings; e.g., chrysene is adsorbed more strongly with phenanthrene;

(2) A compound with more double bonds; e.g., benz(a)anthracene is adsorbed more strongly than pyrene;

(3) An acene (a linearly condensed arene) than for an isomeric phene (an angularly condensed arene); e.g., naphthacene is adsorbed more strongly than benz(a)anthracene;

(4) Fluorenic hydrocarbons than for pericondensed hydrocarbons with the same number of rings and double bonds; e.g., 11H-benzo(b)fluorene is adsorbed more strongly than pyrene;

(5) The most nearly coplanar compound of a group; e.g., the decreasing order of adsorbability, 2-phenylanthracene>1-phenylanthracene>9-phenylanthracene, follows the increasing angle of twist in these molecules;

(6) A hydrocarbon substituted with an increasing number of sterically unhindered methyl or alkylene groups than for the hydrocarbon itself; e.g., 9-methylanthracene is adsorbed more strongly than anthracene; and

(7) The most extensively conjugated isomer; e.g., 1-(2-naphthyl)cyclopentene is adsorbed more strongly than 3-(2-naphthyl)cyclopentene.

It is postulated that adsorption on alumina involves pi-type complexation where the active sites on the alumina are relatively broad electron-attracting areas to which the electron-donating hydrocarbon substrate is held monomolecularly and preferentially in a planar configuration parallel to the surface, if such arrangement is sterically possible.

In general, the columns and techniques used are compromises between better separations and analytical speed.[59,151,195,200,209,210] For example, the cyclohexane elution of an air sample can take two weeks and require 500 to 600 fractions totaling 5,000 ml. To speed up the process it is customary to add increasing amounts of ethyl ether. This speeds the removal of solutes from the column but at the expense of resolution.[59] The chromatographic separation can also be speeded by the use of alumina deactivated by the addition of 1.6 to 1.8 percent water. If the alumina were not deactivated to this extent, the PAH would come off the column too slowly.[59]

Hydrocarbons are eluted in the following order:[210] aliphatics, olefins, benzene derivatives, naphthalene derivatives, dibenzofuran fraction, anthracene fraction, pyrene fraction, benzofluorene fraction, chrysene fraction, benzopyrene fraction, benzoperylene fraction, and coronene fraction. For example, with alumina containing 13.7 percent water, the pyrene fraction was found in the beginning of the 3 percent ether eluent; the chrysene fraction followed in the last part of the 3 percent ether eluent; the benzopyrene fraction appeared in the beginning of the 6 percent ether eluent, followed by the benzoperylene fraction in the start of the 9 percent ether eluent, and the coronene fraction shortly afterward in the same 9 percent ether eluent. Although the relative location of the fractions was always the same, unknown variables sometimes caused the fractions to elute sooner or later than expected. The fractions were fairly well separated, although test tubes containing the tail end of one fraction usually contained small amounts of the next fraction. Most fractions were found in three to six tubes. However, the benzoperylene and coronene fractions were each spread over 6 to 10 tubes.

Column chromatography studies have also been reported by Sawicki et al.,[195,200] in which the separation of polynuclear aza-heterocyclic hydrocarbons and polynuclear aromatic amines was considered. The procedures are essentially the same as for PAH. However, the alumina does cause some decomposition of the amines; e.g., 9-aminoanthracene is recovered in 70 percent yield as anthraquinone, while 2-aminoanthracene is in only 26 percent yield.

6.3.2 Thin-Layer Chromatography

In his 1964 review Sawicki[187] noted that although thin-layer chromatography had been applied only to a small extent in the separation of PAH, it would find increased use; since that time there have been a sizable number of thin-layer chromatography (TLC) studies reported.[13-15,143,191-208,234,277] The advantages of this technique are that it is simple, rapid, inexpensive, sensitive, requires little working material, and can resolve complex mixtures.[187]

Various adsorbents, including silica gel, alumina, cellulose, and cellulose acetate, along with differing types of developing solvents have been evaluated for use in TLC. Several authors[59,143,200,277] state that the complete analysis procedure generally consists of extraction followed by separation using either TLC or paper chromatography, and then spot location by fluorescence or color development.[193] One reagent used for color development is 7,7,8,8-tetracyanoquinodimethan, which reacts with polynuclear compounds to form colored pi complexes.

White and Howard[277] give R_F values (the ratio of the migration distance of the substance to the migration distance of the solvent front) for 29 PAH on cellulose and cellulose acetate adsorbents. Such values, however, are quite specific for a given adsorbent and developing solvent. The R_F values alone are inadequate for characterizing polynuclear compounds.[207]

The efficiency of separation and recovery by TLC has also been studied.[13,202,206,234] Typical results are those reported by Sawicki _et al_.[202,206] in which recoveries of 65 percent for 9-acridanone and 85 percent for BaP were obtained. Assays for these same compounds were also run using fluorometric procedures after TLC separation. It was possible to detect 9-acridanone in concentrations of .0004 ug/m³.[202] For BaP the identification limit ranged between zero and .04 ug.[206]

Previously Sawicki and Johnson[192] had reported the following identification limits: anthracene, 0.01 μg; phenanthrene, 1.0 ug; fluoranthrene, 0.01 ug; chrysene, 0.01 ug; pyrene, 0.001 ug; and BaP, 0.001 μg.

The separation and characterization of polynuclear aza-heterocyclic hydrocarbons and polynuclear aromatic amines have also been reported.[14,15,204,208] The identification limits are in the same range as for PAH; examples are: carbazole, 0.02 μg; 11H-benzo(a)carbazole, 0.02 ug; 1-azacarbazole, 0.2 μg; and 1,2-dinaphthylamine, 0.1 ug.

6.3.3 Gas Chromatography

A limited number of gas chromatography studies have been conducted.[31-33,53,67,279] Although the procedures are still in the process of being worked out, the method promises to be relatively rapid, provided the various chromatographic peaks have been identified. As an example of the capabilities of the method, the following amounts of PAH in soot have been reported:[33] acenaphthylene, 4,700 ug/g soot; phenanthrene, 5,500 ug/g soot; fluoranthrene, 5,200 ug/g soot; chrysene, 6,300 ug/g soot; and BaP, 2,900 ug/g soot.

6.3.4 Other Techniques

Electrophoresis has also been considered a possible means of separating pollutants after collection.[82,212]

Reports show that separations of polynuclear phenols[212] and of macromolecular material[82] are feasible; however, no quantitative information is given.

6.4 Analysis

Analyses of the eluate fractions from chromatography are conducted chiefly via ultraviolet absorption measurements or fluorescence measurements.[187] Presently, the National Air Pollution Control Administration[36] analyzes airborne particulates for BaP by a fluorescence method (a modification of the one described by Sawicki *et al.*[210]) using thin-layer chromatography for separation (see References 234 and 206).

The following discussion briefly reviews the various analytical procedures that are applicable to the study of airborne carcinogens.

6.4.1 Spectral Methods

Methods based on ultraviolet-visible absorption spectra and fluorescence spectra play a prominent role in the identification and determination of polynuclear hydrocarbons. The advantages of absorption spectra are that the wavelength maximum of a compound is unaffected by the presence of other compounds, quenching effects are absent, and the absorption curves of many PAH are available in the literature. The main disadvantage, compared to fluorescence, is the lower sensitivity. For many fluorescent compounds, the excitation and emission spectra are 10 to 10,000 times more sensitive than their absorption spectrum. The disadvantages of fluorescence spectra are the poorer reproducibility, the fewer available quantitative spectra, and quenching that can drastically affect the sensitivity and shape of the spectral curve.[187]

Several recent articles have dealt with spectral methods. Of these, one was a preliminary communication concerned with the detection of impurities in commercial polycyclic hydrocarbon samples.[259] The remaining articles are concerned with the methods of ultraviolet-visible spectra[118,129,156,189,216] and fluorescence spectra.[194,205] The results of these studies are summarized in Table 3.

6.4.2 Other Methods

In one study, Sawicki *et al*.[216] also investigated the application of the piperonal test to the benzene-soluble fraction of airborne particulates. Piperonal reacts with aromatic compounds to give a colored product which obeys Beer's law. The correlation coefficients between BaP concentrations and the piperonal test were 0.95 for 174 urban samples and 0.89 for 25 nonurban samples.

Two papers deal with thermochromic tests for determining the amounts of polynuclear compounds containing the fluorenic methylene group[190] and polycyclic p-quinones.[203]

TABLE 3

SUMMARY OF RECENT INVESTIGATIONS IN SPECTRAL METHODS

Method	Compound(s)	Procedure	Normal Range of Sensitivity	Reference
Ultraviolet	Benzo(a)pyrene	Column chromatography	1 to 6 μg/ml	156
Ultraviolet	Dibenz [a,j]-anthracene	Hexane extraction	0.5 to 5 μg/ml	118
Ultraviolet	Benzo(a)pyrene	Benzene extraction	0 to 45 μg/1,000 /m^3 air	216
Ultraviolet	Benzo(a)pyrene	Hexane extraction	10^{-2} μg/ml	129
Ultraviolet	Benzo(a)pyrene Pyrene Perylene	Modified Piperonal tests	0.003 μ moles/ml 0.01 μ moles/ml 0.001 μ moles/ml	189
Fluorescence	Benzo(a)pyrene Perylene	Acetophenone-trifluoroacetic acid	2.5×10^{-6} M 10^{-6} M	205
Fluorescence	Perylene Anthanthrene Benzo(a)pyrene	Pentane extraction	0.3 μg/ml 0.3 μg/ml 0.4 μg/ml	194

In both cases borohydrides were used at reflux temperatures for color development. Identification limits ranged from 3 to 40 µg. A somewhat similar study was reported in which 4-azobenzenediazonium fluoroborate was used to develop color in the determination of aniline, naphthylamine, and anthramine derivatives. The identification limits were in the range of 2 to 20 µg.

A direct method of determining BaP has been devised using its characteristic quasi-line emission spectrum at liquid nitrogen temperatures.[160] The method has been used to determine BaP in the air of submarine crew quarters, typically about 1 ppm.

Bioassay techniques have been reported in which the response of a microorganism is correlated with carcinogenic activity.[63,65,66,282] These techniques are based on the phenomenon known as photodynamic action where a combination of light energy and chemical sensitizer (in this case PAH) causes the immobilization and death of Paramecium caudatum. Definitive assay for BaP can be performed in the 0.001 to 100 ug/ml region.[66]

7. SUMMARY AND CONCLUSIONS

Epidemiological studies indicate a possible relationship between air pollution and lung cancer mortality in the United States and other countries. While the role of cigarette smoking is clearly better defined, the role of air pollution and possibly of organic carcinogens is less certain but is still believed to be present. The existence of urban-rural differentials and migrant-native differentials speak of a possible contribution of air pollution to total lung cancer mortality.

Animal experiments indicate that under certain conditions many of the organic carcinogens found in ambient air can produce tumors. In most of the experiments, the compounds were painted on the skin. However, these investigations have shown that synergistic and antagonistic effects are important. Thus, some compounds, such as phenols, have been found capable of promoting or reinforcing the action of organic carcinogens. Inhalation experiments indicate that benzo(a)pyrene (BaP) adsorbed on inert particulates (iron oxide) causes a higher incidence of lung tumors in hamsters than just BaP alone. Moreover, these tumors were of the same types observed in humans. In contrast, many noncarcinogenic polynuclear aromatic hydrocarbons (PAH) can reduce the potency of organic carcinogens, at times to such an extent that no effect is found.

No information has been found in the literature concerning the effects of airborne organic carcinogens on plants or materials.

The atmospheric carcinogens fall into three principal categories, namely, PAH, polynuclear heterocyclics and oxygenated compounds, and alkylating agents. There are very little data available on cocarcinogens and anticarcinogens that may be present in the air.

The major sources of PAH are heat generation, refuse burning, industrial processes, and motor vehicles. Of these, heat generation accounts for more than 85 percent of the PAH emitted, with the other three sources each accounting for about 5 percent of the total. Similar figures for other organic carcinogens have not yet been estimated.

Sources of aza-heterocyclics and polynuclear carbonyl compounds have not been well established. Combustion products such as coal tar are likely sources.

Only limited data are available on the concentration of organic carcinogens in the ambient air. In 1966, the concentrations of BaP in 106 urban and nonurban areas were measured. The average value was 0.00279 $\mu g/m^3$ for urban areas and 0.00035 $\mu g/m^3$ for nonurban areas. Other data indicate that BaP constitutes only a small percentage (as low as 5 percent) of the total PAH present in the atmosphere.

Control methods for organic carcinogens are being studied in connection with hydrocarbon and particulate control programs.

The costs of premature death attributable to air pollution and the associated costs of treatment and burial have been estimated. These costs for cancer of the respiratory system were estimated to be $680 million per year on the basis of 1958 data. However, no information has been found on the economic costs of organic carcinogen air pollution or on the costs of its abatement.

Determination of organic carcinogens (mainly PAH) commonly involves separation of the different PAH by chromatographic techniques, followed by analysis by ultraviolet-visible absorption spectra, fluorescence spectra, or phosphorescence spectra.

Based on the material presented in this report, further studies are suggested in the following areas:

(1) Expansion of current efforts to determine the atmospheric concentrations of organic carcinogens. Specific airborne carcinogenic material as well as the composition of hydrocarbon mixtures should be identified. Particle size and geographical distribution should also be determined.

(2) Expansion of animal research to resolve the role of airborne carcinogens, cocarcinogens, and anticarcinogens in pulmonary human cancer.

(3) Determine the significance of the role of organic carcinogens in the so-called "urban factor."

REFERENCES

1. Adams, D.F., The Effects of Air Pollution on Plant Life, A.M.A. Arch. Ind. Health 14:229 (1956).

2. Aigina, E.P., and I.M. Mints, Determination of Low 3,4-Benzpyrene Concentration by Means of the Sbpol'skii Effect, Hyg. Sanitation 31:264 (1966).

3. Air Quality Criteria for Particulate Matter, U.S. Public Health Serv. Publ. AP-49 (1969).

4. Air Quality Data from the National Air Sampling Networks and Contributing State and Local Networks, 1964-1965, U.S. Dept. of Health, Education, and Welfare, Public Health Service, Cincinnati, Ohio (1966).

5. Alarcon, D.G., Demography of Cancer of the Lung, Diseases of the Chest 36:455 (1959).

6. Allison, A.C., and L. Mallucci, Uptake of Hydrocarbon Carcinogens by Lysosomes, Nature 203:1024 (1964).

7. Anderson, M.D., and R.J. Coffey, The Declining Incidence of Carcinoma of the Stomach, Georgetown Med. Bull. 17:201-207 (1964).

8. Ashley, D.J.B., The Distribution of Lung Cancer and Bronchitis in England and Wales, Brit. J. Cancer 21:243 (1967).

9. Badger, G.M., The Carcinogenic Hydrocarbons: Chemical Constitution and Carcinogenic Activity, Brit. J. Cancer 2:309 (1948).

10. Badger, G.M., Mode of Formation of Carcinogens in Human Environment, Natl. Cancer Inst. Monograph 9:1 (1962).

11. Badger, G.M., J.K. Donnelly, and T.M. Spotswood, The Formation of Aromatic Hydrocarbons at High Temperature, Australian J. Chem. 19:1023 (1965).

12. Begeman, C.R., Carcinogenic Aromatic Hydrocarbons in Automobile Effluents, Presented at Congress of Society of Automotive Engineers, Detroit, Mich. (Jan. 8-12, 1962).

13. Bender, D.F., and E. Sawicki, Differentiation of Benzofluorenes on Thin-Layer Substrates, Chemist-Analyst 54:73 (1965).

14. Bender, D.F., E. Sawicki, and R.M. Wilson, Characterization of Carazole and Polynuclear Carbazoles in Urban Air and in Air Polluted by Coal Tar Pitch Fumes by Thin-Layer Chromatography and Spectrophotofluorometry, Intern. J. Air Water Pollution 8:633 (1964).

15. Bender, D.F., E. Sawicki, and R.M. Wilson, Fluorescent Detection and Spectrophotofluorometric Characterization and Estimation of Carazole and Polynuclear Carbazoles Separated by Thin-Layer Chromatography, Anal. Chem. 36:1011 (1964).

16. Bils, R.F., Ultrastructural Alterations of Alveolar Tissue of Mice. I. Due to Heavy Los Angeles Smog, Arch. Environ. Health 12:689 (1966).

17. Bogacz, J., and I. Kiprowski, A Cyto-Pathologic Study of Potentially Carcinogenic Properties of Air Pollutants, Acta Cytol. 5(5):311 (1961).

18. Bosco, G., et al., Determination of Aromatic Polycyclic Hydrocarbons in the Atmospheric Dust of the City of Siena, in Italian, Nuovi Ann. Ig. Microbiol. 17:297 (1966).

19. Boubel, R.W., and L.A. Ripperton, Benzo(a)pyrene Production During Controlled Combustion, J. Air Pollution Control Assoc. 13:553 (1963).

20. Brandt, C.S., and W.W. Heck, "Effects of Air Pollution on Plants," in Air Pollution, vol. 1, 2nd ed., A.C. Stern, Ed. (New York: Academic Press, pp. 401-43,1968).

21. Bregeman, C.R., Carcinogenic Aromatic Hydrocarbons in Automobile Effluents, Automotive Engineering Congress, Society of Automotive Engineers, Detroit, Mich. (Jan. 8-12, 1962).

22. Buck, S.F., and A.J. Wicken, Report on a Study of Environmental Factors Associated with Lung Cancer and Bronchitis Mortality in Areas of North East England, Tobacco Research Council, London, Research Paper 8 (1964).

23. Buell, P., and J.E. Dunn, Relative Impact of Smoking and Air Pollution on Lung Cancer, Arch. Environ. Health 15:291 (1967).

24. Buell, P., J.E. Dunn, and L. Breslow, Cancer of the Lung and Los Angeles-Type Air Pollution. Prospective Study, Cancer 20: 2139 (1967).

25. Burrows, I.E., and A.J. Lindsey, Hydrocarbons by Pyrolysis of Simple Aliphatic Hydrocarbons, Chem. Ind. (London) p. 1395 (1961).

26. California Standards for Ambient Air Quality and Motor Vehicle Exhaust, State of California Department of Health Technical Report, Berkeley, Calif. (1960).

27. Campbell, J.A., Cancer of Skin and Increase in Incidence of Primary Tumours of Lung in Mice Exposed to Dust Obtained from Tarred Roads, Brit. J. Exptl. Pathol. 15:287 (1934).

28. Campbell, J.A., Carcinogenic Agents Present in Atmosphere and Incidence of Primary Lung Tumours in Mice, Brit. J. Exptl. Pathol. 20:122 (1939).

29. Campbell, J.M., and J. Clemmesen, Benzopyrene and Other Polycyclic Hydrocarbons in the Air of Copenhagen, Danish Med. Bull. 3:205 (1956).

30. Campbell, J.M. and L. Kreyberg, The Degree of Air Pollution in Norwegian Towns, Brit. J. Cancer 10:481 (1956).

31. Cantuti, V., G.P. Cartoni, A. Liberti, and A.G. Torri, Improved Evaluation of Polynuclear Hydrocarbons in Atmospheric Dust by Gas Chromatography, J. Chromatog. 17:60 (1965).

32. Carugno, N., and S. Rossi, Evaluation of Polynuclear Hydrocarbons in Cigaret Smoke by Glass Capillary Columns, J. Gas Chromatog. 5:103 (1967).

33. Chakraborty, B.B., and R. Long, Gas Chromatographic Analysis of Polycyclic Aromatic Hydrocarbons in Soot Samples, Environ. Sci. Tech. 1:828 (1967).

34. Clarke, J.M., The Problem of Cancer in New Zealand, New Zealand Med. J. 63:788 (1964).

35. Cleary, G.J., and J.L. Sullivan, Pollution by Polycyclic Aromatic Hydrocarbons in the City of Sydney, Med. J. Australia 1:758 (1965).

36. Clements, J.B., National Air Pollution Control Administration, Cincinnati, Ohio, personal communication (Aug. 1968).

37. Clemmesen, J., A. Nielsen, and E. Jensen, The Increase in Incidence of Carcinoma of the Lung in Denmark, Brit. J. Cancer 7:1 (1953).

38. Clemo, G.R., and E.W. Miller, Carcinogenic Action of City Smoke, Chem. Ind. (London) p. 38 (1955).

39. Colucci, J.M., and C.R. Begeman, The Automotive Contribution to Air-borne Polynuclear Aromatic Hydrocarbons in Detroit, J. Air Pollution Control Assoc. 15:113 (1965).

40. Crabtree, H.C., Retardation of the Rate of Tumor Induction by Substances Which Inhibit Glycolysis, J. Pathol. Bacteriol. 51:303 (1940).

41. Crocker, T.T., B.I. Nielsen, and I. Lasnitzki, Carcinogenic Hydrocarbons, Arch. Environ. Health 10:240 (1965).

42. Curwen, M.P., E.L. Kennaway, and N.M. Kennaway, The Incidence of Cancer of the Lung and Larynx in Urban and Rural Districts, Brit. J. Cancer 8:181 (1954).

43. Dahlman, T., M.L. Edfors, and R. Rylander, Retention of Cigarette Smoke Components in Human Lungs, Arch. Environ. Health 17:746 (1968).

44. Daines, R.H., I.A. Leone, and E.G. Brennan, Air Pollution and Its Effect on Agriculture in New Jersey, New Jersey Agr. Expt. Sta. Bull. 794:1 (1960).

45. Danetskaya, O.L., and P.P. Dikun, Hyg. Sanitation 29:121 (1964).

46. Darley, E.F., C.W. Nichols, and J.T. Middleton, Identification of Air Pollution Damage to Agricultural Crops, Calif. Dept. Agr. Bull. 55:11 (1966).

47. Dautrebande, L., H. Beckman, and W. Walkenhorst, Lung Deposition of Fine Dust Particles, A.M.A. Arch. Ind. Hyg. 16:179 (1957).

48. Davies, J.W., C.B. Walker, and E.W. Best, The Magnitude of the Lung Cancer Problem in Canada, Can. Med. Assoc. J. 89:1084 (1963).

49. Dean, G., Lung Cancer Among White South Africans, Brit. Med. J. II:852 (1959).

50. Dean, G., Lung Cancer Among White South Africans, Report on a Further Study, Brit. Med. J. 5267:1599 (1961).

51. Dean, G., Lung Cancer in Australia, Med. J. Australia 49:1003 (1962).

52. DeGraaf, H., and V.W. Keuringsdienst, Rotterdam, Commissie, Boden, Water en Lucht (1961): cited by Sawicki, Ref. 40.

53. DeMaio, L., and M. Corn, Gas Chromatographic Analysis of Polynuclear Aromatic Hydrocarbons with Packed Columns: Application to Air Pollution Studies, Anal. Chem. 38:131 (1966).

54. Diehl, E.K., F. duBreuil, and R.A. Glenn, Eng. Power (1966).

55. Doll, R., and A.B. Hill, Smoking and Carcinoma of the Lung, Brit. Med. J. 2:739 (1950).

56. Doll, R., and A.B. Hill, A Study of the Aetiology of Carcinoma of the Lung, Brit. Med. J. 2:1271 (1952).

57. Dorn, H.F., Le Cancer chez les Animaux Domestiques en Turquie, Acta Unio Intern. Contra Cancrum 9:126 (1953).

58. Dubois, L., A. Zdrojewski, and J.L. Monkman, Comparison of Three Methods for Trace Analysis of Polycyclics, Mikrochim. Acta 5:903 (1967).

59. Dubois, L., A. Zdrojewski, C. Baker, and J.L. Monkman, Some Improvements in the Determination of Benzo(a)pyrene in Air Samples, J. Air Pollution Control Assoc. 17:818 (1967).

60. Dunn, H.L., Lung Cancer in the Twentieth Century, J. Intern. Coll. Surgeons 23:326 (1955).

61. Eastcott, D.F., The Epidemiology of Lung Cancer in New Zealand, Lancet 1:37 (1956).

62. Eastcott, D.F., in The Air We Breathe, S.M. Farber and R.H.L. Wilson, Eds. (Springfield, Ill.: Thomas, pp. 351-369, 1961).

63. Epstein, S.S., Photoactivation of Polynuclear Hydrocarbons, Arch. Environ. Health 10:233 (1965).

64. Epstein, S.S., Carcinogenicity of Organic Extracts of Atmospheric Pollutants, J. Air Pollution Control Assoc. 17:(11)728 (1967).

65. Epstein, S.S., M. Small, J. Kiplan, N. Mantel, H.L. Falk, and E. Sawicki, Photodynamic Bioassary of Polycyclic Air Pollutants, Arch. Environ. Health 7:531 (1963).

66. Epstein, S.S., M. Small, E. Sawicki, and H.L. Falk, Photodynamic Bioassay of Polycyclic Atmospheric Pollutants, J. Air Pollution Control Assoc. 15:174 (1965).

67. Ettre, L.S., R.D. Condon, F.J. Kabot, and E.W. Cieplinski, Dual Column-Differential Flame Ionization Detector System and Its Application with Packed and Golay Type Columns, J. Chromatog. 13:305 (1964).

68. Falk, H.L., Institute of Environmental Health Services, Research Triangle Park, Durham, N.C., personal communication (Aug. 1969).

69. Falk, H.L., P. Kotin, and A. Miller, Aromatic Polycyclic Hydrocarbons in Polluted Air as Indicators of Carcinogenic Hazards, Intern. J. Air Pollution 2:201 (1960).

70. Falk, H.L., A. Miller, and P. Kotin, The Elusion of 3,4-Benzpyrene and Related Hydrocarbons from Soot by Plasma Proteins, Science 127:474 (1958).

71. Fenner, M.L. and J. Braven, The Mechanism of Carcinogenesis by Tobacco Smoke. Further Experimental Evidence and a Prediction from the Thiol-Defence Hypothesis, Brit. J. Cancer 22:474 (1968).

72. Food Protection Comm. Food Nutr. Board, Natl. Acad. Sci.--Natl. Res. Council, Publ. 749 (1959).

73. Frank, A., and G. Gerhardsson, Some Studies of 3,4-Benzopyrene in Stockholm, Nord. Hyg. Tidskr. 43:42 (1962).

74. Fraumeni, J.F., Cigarette Smoking and Cancers of the Urinary Tract: Geographic Variation in the United States, J. Natl. Cancer Inst. 41:1205 (1968)

75. Friberg, L. (Chairman), Medical Air Quality Criteria for Standards (In Sweden), National Swedish Committee for Air Purification, Sattsjobaden, Sweden, May 27-29, 1964 and National Institute of Public Health, Stockholm, Sweden, June 11, 1964. APTIC Document 10199.

76. Galuskinova, V., 3,4-Benzpyrene Determination in the Smoky Atmosphere of Social Meeting Rooms and Restaurants. A Contribution to the Problem of the Noxiousness of So-Called Passive Smoking, Neoplasma 11:465 (1964).

77. Gardner, M.B., Biological Effects of Urban Air Pollution. 3. Lung Tumors in Mice, Arch. Environ. Health 12:305 (1966).

78. Giovanella, B.C., L.E. McKinney, and C. Heidelberger, On the Reported Solubilization of Carcinogenic Hydrocarbons in Aqueous Solutions of DNA, J. Mol. Biol 8:20 (1964).

79. Gofmekler, V.A., M.D. Manita, Zh.V. Manusadzhants, and L.P. Stepanov, Hyg. Sanitation 28:(3) 3 (1963).

80. Goldman, K.P., Mortality of Coal-Miners from Carcinoma of the Lung, Brit. J. Ind. Med. 22:72 (1965).

81. Goos, A.W., in Wood Chemistry, L.E. Wise and E.C. Jahn, Eds. (New York: Reinhold, p. 817, 1952).

82. Goppers, V., and H.J. Paulus, Macromolecular Compounds Isolated from Airborne Particles by Electrophoresis and Paper Chromatography, Am. Ind. Hyg. Assoc. J. 23:181 (1962).

83. Gorman, E., Med. Officer 101:178 (1959).

84. Gurinov, B.P., V.N. Tugarinova, O.I. Vasil'yeva, M.V. Nifontova, and L.M. Shabad, On the Carcinogenic Properties of Exhaust Carbon from Motor Transport, Hyg. Sanitation 27: 19 (1962).

85. Haenszel, W., Cancer Mortality Among Foreign-born in the United States, J. Natl. Cancer Inst. 26:37 (1961).

86. Haenszel, W., D.B. Loveland, and M.G. Sirken, Lung-Cancer Mortality as Related to Residence and Smoking Histories. I. White Males, J. Natl. Cancer Inst. 28:947 (1962).

87. Hammond, E.C., and D. Horn, The Relationship Between Human Smoking Habits and Death Rates, J. Am. Med. Assoc. 155:1316 (1954).

88. Hammond, E.C., and D. Horn, Smoking and Death Rates--Report on 44 Months of Follow-up of 187,783 Men, J. Am. Med. Assoc. 166:1 (1958).

89. Hangebrauck, R.P., R.P. Lauch, and J.E. Meeker, Emissions of Polynuclear Hydrocarbons from Automobiles and Trucks, Am. Ind. Hyg. Assoc. 27:47 (1966).

90. Hangebrauck, R.P., D.J. vonLehmden, and J.E. Meeker, Emissions of Polynuclear Hydrocarbons and Other Pollutants from Heat-Generation and Incineration Processes, J. Air Pollution Control Assoc. 14:267 (1964).

91. Hangebrauck, R.P., D.J. vonLehmden, and J.E. Meeker, Sources of Polynuclear Hydrocarbons in the Atmosphere, U.S. Public Health Serv. Publ. 999-AP-33 (1967).

92. Hansbrough, J.R., Air Quality and Forestry, Proc. AAAS Symp. Agr. and Quality of Our Environment, Washington, D.C., 1966 (1968).

93. Harington, J.S., Chemical Studies of Abestos, Ann. N.Y. Acad. Sci. 132:31 (1965).

94. Harington, J.S., and F.J.C. ROE Studies of Carcinogenesis of Abestos Fibers and Their Natural Oils, Ann. N.Y. Acad. Sci. 132:439 (1965).

95. The Health Consequences of Smoking, U.S. Public Health Serv. Publ. 1696. (1967)

96. Hendrickson, E.R., C.G. Walker, and V.D. Chapnereskar, Identification of Non-Sulfer Organic Compounds in Stack Gases from Pulp Mills, Am. Ind. Hyg. Assoc. J. 24:121 (1963).

97. Hepting, G.H., Damage to Forests from Air Pollution, J. Forestry 63:630 (1964).

98. Herrold, K. McD., The Effects of Benzo(a)pyrene, Cigarette Smoke Condensate and Atmospheric Pollutants on the Respiratory System of Syrian Hamsters, Acta Union Intern. Contre Le Cancer 19 (3-4):710 (1963).

99. Herrold, K. McD., and L.J. Dunham, Induction of Carcinoma and Pipilloma on the Tracheobronchial Mucosa of the Syrian Hamster by Intratracheal Instillation of Benzo(a)pyrene. J. Cancer Inst. 28:467 (1962).

100. Heuche, H.O., Intern. J. Air Water Pollution 8:185 (1964).

101. Hinch, N., Air Pollution, J. Chem. Educ. 46:93 (1969).

102. Hoffman, E.F., and A.G. Gilliam, Lung Cancer Mortality: Geographic Distribution in the United States, 1948-1949, Public Health Rept. (U.S.) 69:1033 (1954).

103. Hoffmann, D., and E.L. Wynder, in Air Pollution vol. II, 2nd ed., A.C. Stern, Ed. (New York: Academic Press, Chap. 20, 1960).

104. Hoffmann, D., and E.L. Wynder, A Study of Air Pollution Carcinogenesis. II. Carcinogenic Activity of Gasoline Engine Exhaust Condensate, Cancer 15:103 (1962).

105. Hoffmann, D., E. Theisz, and E.L. Wynder, Studies on the Carcinogenicity of Gasoline Exhaust, J. Air Pollution Control Assoc. 15:162 (1965).

106. Hsu, W.T., J.W. Moohr, and S.B. Weiss, Proc. Natl. Acad. Sci. 53:517 (1965).

107. Hsu, W.T., J.W. Moohr, A.Y.M. Tsai, and S.B. Weiss, The Influence of Polycyclic Aromatic Hydrocarbons on Bacteriophage Development. II. Proc. Natl. Acad. Sci. 55:1475 (1966).

108. Hueper, W.C., A Quest Into the Environmental Causes of Cancer of the Lung, U.S. Public Health Monograph 36 (1955).

109. Hueper, W.C., P. Kotin, E.C. Tabor, W.W. Payne, H. Falk, and E. Sawicki, Carcinogenic Bioassays on Air Pollutants, Arch. Pathol. 74:89 (1962).

110. Hueter, F.G., G.L. Contner, K.A. Bisch, and R.G. Hinners, Biological Effects of Atmospheres Contaminated by Auto Exhaust, Arch. Environ. Health 12:533 (1966).

111. Il'nitskii, A.P., and S.N. Varshavskaya, Water as a Factor in Spreading Carcinogens in the Environment, Hyg. Sanitation 29:88 (1965).

112. Jaffe, L.S., Photochemical Air Pollutants and Their Effects on Men and Animals. I. General Characteristics and Community Concentrations, Arch. Environ. Health 15:782 (1967).

113. Jaffe, L.S., Photochemical Air Pollutants and Their Effect on Men and Animals. II. Adverse Effects, Arch. Environ. Health 16:241 (1968).

114. Just, J., et al., Studies on the Composition and Properties of Carcinogenic Material Contained in the Dust in the Atmospheric Air. I. Content of Benzo(a)pyrene and Other Polycyclic Hydrocarbons in the Atmospheric Dust of Ten Polish Cities, in Polish, Roczn. Panstiv. Zakl. Hig. 18:637 (1967).

115. Kennaway, E.L., and N.M. Kennaway, The Incidence of Cancer of the Lung in Coal Miners in England and Wales, Brit. J. Cancer 7:10 (1953).

116. Kireeva, I.S., Atmospheric Pollution with 3,4-Benzpyrene in Vicinity of a Coal Briquette Factory, Hyg. Sanitation 30(7):126 (1967).

117. Konstantinova, A.I., and N.D. Chertova, Lung Cancer Morbidity in Relation to Air Pollution, in Russian, J. Klini ChesKaya Meditsina (Clinical Medicine) XL (12):104 (1962).

118. Korotkov, P.A., N.N. Serzhantov, Yu P. Tsyaschchenko, and N.Ya. Yanysheva, Determination of Small Concentrations of 1,2,5,6-Dibenzanthracene, Hyg. Sanitation 29:59 (1964).

119. Kotin, P., and L. Falk, Atmospheric Factors in Pathogenesis of Lung Cancer, Advan. Cancer Res. 7:475 (1963).

120. Kotin, P., and H.L. Falk, The Role and Action of Environmental Agents in the Pathogenesis of Lung Cancer. I. Air Pollutants, Cancer 12:147 (1959).

121. Kotin, P., and H.L. Falk, Air Pollution and Lung Cancer, Presented at the National Conference on Air Pollution, Paper C-5 (Dec. 11, 1962).

122. Kotin, P., and H.L. Falk, Organic Peroxides, Hydrogen Peroxide, Epoxides, and Neoplasia, Radiation Res. Suppl. 3:193 (1963).

123. Kotin, P., and D.V. Wiseley, "Production of Lung Cancer in Mice by Inhalation Exposure to Influenza Virus and Aerosols of Hydrocarbons," in Progress in Experimental Tumor Research, Vol. III, F. Homburger, Ed. (Basel: Karger, 1962).

124. Kotin, P., H.L. Falk, and M. Thomas, Aromatic Hydrocarbons; Presence in Particulate Phase of Diesel-Engine Exhausts and Carcinogenicity of Exhaust Extracts, Arch. Ind. Health 11: 113 (1955).

125. Kotin, P., H.L. Falk, and M. Thomas, Production of Skin Tumors in Mice with Oxidation Products of Aliphatic Hydrocarbons, Cancer 9:910 (1956).

126. Kotin, P., H.L. Falk, W. Lijinsky, and L. Zechmeister, Inhibition of the Effect of Some Carcinogens by Their Partially Hydrogenated Derivatives, Science 123:102 (1956).

127. Kotin, P., H.L. Falk, P. Mader, and M. Thomas, Ind. Hyg. Occupational Med. 9:153 (1964).

128. Kreyberg, L., Occurrence and Aetiology of Lung Cancer in Norway in the Light of Pathological Anatomy, Brit. J. Prevent. & Social Med. 10:145 (1956).

129. Krotkov, P.A., N.N. Serzhantova, and V.B. Timofeev, A Photoelectrometric Method for the Determination of Low 3,4-Benzpyrene Concentrations, Hyg. Sanitation 28:47 (1963).

130. Kuschner, M., S. Laskin, E. Cristofano, and N. Nelson, in Proc. Third Natl. Cancer Conf. (Philadelphia: Lippincott, p. 485, 1956).

131. Kutscher, W., and R. Tomingas, Atmospheric Dusts and Soot in the Mannheim Area, Staub. 26 (1966).

132. Lacassagne, A., N.P. Buu-Hoi, and G. Rudali, Inhibition of the Carcinogenic Action Produced by a Weekly Carcinogenic Hydrocarbon on a Highly Active Carcinogenic Hydrocarbon, Brit. J. Exptl. Pathol. 26:5 (1945).

133. Lacassagne, A., F. Zajdela, N.P. Buu-Hoi, O. Chalvet, and G.H. Daub, Eleven Active Carcinogens of Mono-, Di-, and Tri-methylbenzo(a)pyrenes, Int. J. Cancer 3:238 (1968).

134. Laskin, S., M. Kuschner, N. Nelson, B. Altshuler, J.H. Hartley, and M. Daniels, Carcinoma of the Lung in Rats Exposed to the Beta-Radiation of Intrabronchial Ruthenium Pellets. I. Dose Response Relationships, J. Natl. Cancer Inst. 31:219 (1963).

135. Lasnitzki, I., Observations on the Effects of Condensates from Cigarette Smoke on Human Foetal Lung in Vitro, Brit. J. Cancer 12:547 (1958).

136. Lasnitzki, I., and E.L. Kennaway, Annual Report, Cambridge, Eng. Strangeways Research Laboratory, p. 22 (1955).

137. Lasnitzki, I., and S.R. Pelc, Effect of 20-Methylcholanthrene on DNA Synthesis in Mouse Prostrates Grown in Vitro, Exptl. Cell Res. 13:140 (1957).

138. Lawther, P.J., and R.E. Waller, Trans. A. Indus. M. Officers 9:5 (Apr. 1959).

139. Lawther, P.J., B.T. Commins, and R.E. Waller, A Study of the Concentrations of Polycyclic Aromatic Hydrocarbons in Gas Works Retort Houses, Brit. J. Ind. Med. 22:13 (1965).

140. Leiter, J., and M.J. Shear, Production of Tumors in Mice with Tars from City Air Dusts, J. Natl. Cancer Inst. 3:167 (1942).

141. Leiter, J., M.B. Shimkin, and M.J. Shear, Production of Subcutaneous Sarcomas in Mice with Tars Extracted from Atmospheric Dusts, J. Natl. Cancer Inst. 3:155 (1942).

142. Lewis, H.R., With Every Breath We Take (New York: Crown, 1965).

143. Lindstedt, G., A Simplified Chromatographic Method for the Routine Determination of 3,4-Benzopyrene in Air Samples, Atmos. Environ. 2:1 (1968).

144. Litvinov, N.N., M.S. Goldberg, and S.N. Kiminia, Morbidity and Mortality in Man Caused by Pulmonary Cancer and Its Relation to the Atmosphere in the Areas of Aluminum Plants, Acta Unio Intern. Contra Cancrum 19:742 (1963).

145. Long, R., Formation of Polycyclic Aromatic Hydrocarbons During Incomplete Combustion, Progress Rept., Oct. 1, 1964-Mar. 31, 1967, Birmingham Univ., Eng. (Mar. 1967).

146. Louw, C.W., The Quantitative Determination of Benzo(a)pyrene in the Air of South African Cities, Am. Ind. Hyg. Assoc. J. 26:520 (1965).

147. Lyons, M.J., and H. Johnston, Chemical Investigation of the Neutral Fraction of Cigarette Smoke Tar, Brit. J. Cancer 11: 554 (1957).

148. Mancuso, T.F., and E.J. Coulter, Cancer Mortality Among Native White, Foreign-Born White, and Nonwhite Male Residents of Ohio: Cancer of the Lung, Larynx, Bladder, and Central Nervous System, J. Natl. Cancer Inst. 20:79 (1958).

149. Middleton, J.T., E.F. Darley, and R.F. Brewer, Damage to Vegetation from Polluted Atmosphere, J. Air Pollution Control Assoc. 8:9 (1958).

150. Moore, G.E., M. Katz, and W.B. Drowley, Polynuclear Aromatic Hydrocarbons in Urban Atmospheres in Ontario, J. Air Pollution Control Assoc. 16:492 (1966).

151. Moore, G.E., R.S. Thomas, and J.L. Monkman, The Routine Determination of Polycyclic Hydrocarbons in Airborne Pollutants, J. Chromotog. 26:456 (1967).

152. Motley, H.L., R.H. Smart and G.I. Leftwich, Effect of Polluted Los Angeles Air (Smog) on Lung Volume Measurements, J. Am. Med. Assoc. 171(11):1469 (1959).

153. Mueller, F.H., Tobacco Misuse and Lung Carcinoma, Z. Krebs Forsch. 49:57 (1939).

154. Neal, J., and R.H. Rigdon, Absorption and Excretion of Benzpyrene When Fed to Mice, Texas Rept. Biol. Med. 22(1):156 (1964).

155. Neal, J., and R.H. Rigdon, Gastric Tumors in Mice Fed Benzo(a)pyrene: A Quantitative Study, Texas Rept. Biol. Med. 25:494 (1965).

156. Nenasheva, S.K., Spectrophotometric Determination of 3,4-Benzpyrene in the Presence of Pyrene, Hyg. Sanitation 31: 213 (1966).

157. Newsome, J.R., and C.H. Keith, Tobacco Sci. 9:65 (1965).

158. Noble, W.M., Smog Damage to Plants, Lasca Leaves 15:1 (1965).

159. Oberdorfer, P.E., The Determination of Aldehydes in Automotive Exhaust Gas, Automotive Engineering Congress, Society of Automotive Engineers, Detroit, Mich. (Jan. 9-13, 1967).

160. Parker, C.A., and W.T. Rees, Determination of 3,4-Benzpyrene in the Atmosphere of a Submarine, AML Report No. A/68(M) Admirality Materials Laboratory, Holton Heath, Poole.

161. Pavelka, F., and A. D'Ambrosio, The 3,4-Benzpyrene Content of the Atmosphere in Milan, Rept. Ammin. Provinc. Milano, p. 111 (1959).

162. Phillips, A.J., Mortality from Cancer of Lung in Canada, 1931-1952, Can. Med. Assoc. J. 71:242 (1954).

163. Pitot, M.C., and C. Heidelberger, Metabolic Regulatory Circuits and Carcinogenesis, Cancer Res. 23:1964 (1963).

164. Poglasova, M.N., G.E. Feeloseeva, A.J. Khesina, M.N. Meissel, and L.M. Shahab, On the Possibility of Benz(a)pyrene Metabolism by Soil Microorganisms, Dokl. Akad. Nauk SSSR 169:1174 (1966).

165. Pybus, F.C., Cancer and Atmospheric Pollution, Med. Proc. 10: 242,268 (1964).

166. Pylev, L.N., Effect of the Dispersion of Soot in Deposition of 3,4-Benzpyrene in Lung Tissue of Rats, Hyg. Sanitation 32:174 (1967).

167. Rakower, J., Lung Cancer in Israel, Cancer 10:67 (1957).

168. Remmers, J.E., and O.J. Balchum, Paper 65-43, Presented at the 58th Annual Meeting, Air Pollution Control Association, Toronto, Can. (June 1965).

169. Ridker, R.G., Economic Costs of Air Pollution (New York: Praeger, 1967).

170. Rigdon, R.H., Pulmonary Neoplasms Produced by Methylcholathrene in the White Peakin Duck, Cancer Res. 21:571 (1961).

171. Rigdon, R.H., and H. Kirchoff, Cancer of the Lung 1930 to 1960: A Review, Texas Rept. Biol. Med. 19:465 (1961).

172. Rigdon, R.H., and J. Neal, Absorption and Excretion of Benzpyrene Observations in the Duck, Chicken, Mouse, and Dog, Texas Rept. Biol. Med. 21(2):247 (1963).

173. Rigdon, R.H., and J. Neal, Gastric Carcinoma and Pulmonary Adenomas on Mice Fed Benzo(a)pyrene, Texas Rept. Biol. Med. 24(2):195 (1966).

174. Rimington, J., Smoking, Sputum, and Lung Cancer, *Brit. Med. J.* 1:732 (1968).

175. Roe, F.J.C., *et al.*, Incomplete Carcinogens in Cigarette Smoke Condensate: Tumor Production by a Phenolic Fraction, *Brit. J. Cancer* *14*:623 (1960).

176. Rondia, D., The Effect of the Fogs of February 1959 on the Concentration of Polycyclic Hydrocarbons in the Atmosphere of the Liege Area, *Arch. Belg. Med. Soc.* *18*:220 (1960).

177. Rothwell, K., and J.K. Whitehead, Complex Formation, Isolation and Carcinogenicity of Polycyclic Aromatic Hydrocarbons, *Nature* *213*:797 (1967).

178. Rounds, D.E., Environmental Influences on Living Cells, *Arch. Environ. Health* *12*:78 (1966).

179. Rounds, D.E., A. Awa, and C.M. Pomerat, Effect of Automobile Exhaust on Cell Growth in Vitro, *Arch. Environ. Health* *5*:319 (1962).

180. Saffiotti, U., F. Cefis, and L.H. Kolb, Bronchogenic Carcinoma Induction by Particulate Carcinogens, *Proc. Am. Assoc. Cancer Res.* *5*(1):55 (1964).

181. Saffiotti, U., F. Cefis, and L.H. Kolb, A Method for the Experimental Induction of Bronchogenic Carcinoma, *Cancer Res.* *28*(1):104 (1969).

182. Saffiotti, U., S.A. Borg, M.L. Grote, and D.B. Karp, Retention Rates of Particulate Carcinogens in the Lungs. Studies in an Experimental Model for Lung Cancer Induction, *Chicago Med. School Quart.* *24*:10 (1964).

183. Saffiotti, U., R. Montesano, A.S. Sellakumar, and S.A. Borg, Experimental Cancer of the Lung. Inhibition by Vitamin A of the Tracheobronchial Squamous Metaplasia and Squamous Cell Tumors, *Cancer* *20*:857 (1967).

184. Saffiotti, U., *et al.*, Experimental Studies of the Conditions of Exposure to Carcinogens for Lung Cancer Induction, *J. Air Pollution Control Assoc.* *15*(1):23 (1965).

185. Saringer, M., *Erdeszeti Geszegtudomany (Budapest)* *7*:25 (1963).

186. Sato, S., and R.J. Cvetanovic, The Effect of Molecular Oxygen on the Reaction of Oxygen Atoms with CIS-2-Pentene, *Can. J. Chem.* *37*:953 (1959).

187. Sawicki, E., Separation and Analysis of Polynuclear Aromatic Hydrocarbons Present in the Human Environment, *Chemist-Analyst* *53*:24, 28, 56, 88 (1964).

188. Sawicki, E., Airborn Carcinogens and Allied Compounds, *Arch. Environ. Health* *14*:46 (1967).

189. Sawicki, E., and R. Barry, New Colorer Tests for the Larger Polynuclear Aromatic Hydrocarbons, *Talanta* *2*:128 (1959).

190. Sawicki, E., and W. Elbert, Thermochromic Detection of Polynuclear Compounds Containing the Fluorenic Methylene Group, *Chemist-Analyst* *48*:68 (1959).

191. Sawicki, E., and H. Johnson, Characterization of Aromatic Compounds by Low-Temperature Fluorescence and Phosphrescence: Application to Air Pollution Studies, *Microchem. J.* *8*:85 (1964).

192. Sawicki, E., and H. Johnson, Thin Layer Chromatographic Characterization Tests for Basic Polynuclear Compounds. Application to Air Pollution, *Mikrochim. Acta* *2*:435 (1964).

193. Sawicki, E., C.R. Engel, and W.C. Elbert, Chromatographic Location and Colorimetric Determination of Mercaptans, Prolines, and Free Radical Precursors, *Talanta* *14*:1169 (1967).

194. Sawicki, E., T.R. Hauser, and T.W. Stanley, Ultraviolet Visible and Fluorescence Spectral Analysis of Polynuclear Hydrocarbons, *Intern. J. Air Pollution* *2*:253 (1960).

195. Sawicki, E., H. Johnson, and K. Kosinski, Chromotographic Separation and Spectral Analysis of Polynuclear Aromatic Amines and Heterocyclic Imines, *Microchem. J.* *10*:72 (1966).

196. Sawicki, E., J.E. Meeker, and M.J. Morgan, Polynuclear Aza Compounds in Automotive Exhaust, *Arch. Environ. Health* *11*:773 (1965).

197. Sawicki, E., J.E. Meeker, and M.J. Morgan, The Quantitative Composition of Air Pollution Source Effluents in Terms of Aza Heterocyclic Compounds and Polynuclear Aromatic Hydrocarbons, *Air Water Pollution* *9*:291 (1965).

198. Sawicki, E., J.L. Noe, and F.T. Fox, Spot Test Detection and Colorimetric Determination of Aniline, Naphthylamine and Anthramine Derivatives with 4-Azobenzenediazonium Fluoroborate, *Talanta* *8*:257 (1961).

199. Sawicki, E., T.W. Stanley, and W.C. Elbert, Quenchofluormetric Analysis for Fluoranthenic Hydrocarbons in the Presence of Other Types of Hydrocarbons, Talanta 11:1433 (1964).

200. Sawicki, E., T.W. Stanley, and W.C. Elbert, Characterization of Polynuclear Aza Heterocyclic Hydrocarbons Separated by Column and Thin-Layer Chromatography From Air Pollution Source Particulates, J. Chromatog. 18:512 (1965).

201. Sawicki, E., T.W. Stanley, and W.C. Elbert. Direct Flurometric Scanning of Thin-Layer Chromatograms and Its Application to Air Pollution Studies, J. Chromatog. 20:348 (1965).

202. Sawicki, E., T.W. Stanley, and W.C. Elbert, Assay for 9-Acridanone in Urban Atmosphere by Thin-Layer Chromatography Fluorimetric Procedures, Talanta 14:431 (1967).

203. Sawicki, E., T.W. Stanley, and T.R. Hauser, Ultraviolet, Visible and Fluorescence Spectral Analysis of Polynuclear Hydrocarbons, Anal. Chem. 30:2005 (1958).

204. Sawicki, E., T.W. Stanley, and H. Johnson, Direct Spectrofluorometric Analysis of Aromatic Compounds on Thin-Layer Chromatograms, Microchem. J. 8:257 (1964).

205. Sawicki, E., T.W. Stanley, and H. Johnson, Quenchofluorometric Analysis for Polynuclear Compounds, Mikrochim. Acta 1:178 (1965).

206. Sawicki, E., T.W. Stanley, W.C. Elbert, and J.D. Pfaff, Application of Thin-Layer Chromatography to the Analysis of Atmospheric Pollutions and Determination of Benzo(a)pyrene, Anal. Chem. 36:497 (1964).

207. Sawicki, E., T.W. Stanley, S. McPherson, and M. Morgan, Use of Gas-Liquid and Thin-Layer Chromatography in Characterizing Air Pollutants by Fluorometry, Talanta, 13:619 (1966).

208. Sawicki, E., T.W. Stanley, J.D. Pfaff, and W.C. Elbert, Thin-Layer Chromatographic Separation and Analysis of Polynuclear Aza Heterocyclic Compounds, Anal. Chim. Acta 31:359 (1964).

209. Sawicki, E., W. Elbert, T.W. Stanley, T.R. Hauser, and F.T. Fox, The Detection and Determination of Polynuclear Hydrocarbons in Urban Airborne Particulates. I. The Benzopyrene Fraction, Intern. J. Air Pollution 2:273 (1960).

210. Sawicki, E., W. Elbert, T.W. Stanley, T.R. Hauser, and F.T. Fox, Separation and Characterization of Polynuclear Aromatic Hydrocarbons in Urban Airborne Particulates, Anal. Chem. 32:810 (1960).

211. Sawicki, E., F.T. Fox, W.C. Elbert, T.R. Hauser, and J.E. Meeker, Polynuclear Aromatic Hydrocarbon Composition of Air Polluted by Coal-Tar Pitch Fumes, Am. Ind. Hyg. Assoc. J. 23:482 (1962).

212. Sawicki, E., M. Guyer, R. Schumacher, W.C. Elbert, and C.R. Engel, Electrophoretic and Chromatographic Separation and Fluorimetric Analysis of Polynuclear Phenols. Application to Air Pollution, Mikrochim. Acta 5:1025 (1968).

213. Sawicki, E., T.R. Hauser, W.C. Elbert, F.T. Fox, and J.E. Meeker, Polynuclear Aromatic Hydrocarbon Composition of Atmosphere in Some Large American Cities, Am. Ind. Hyg. Assoc. J. 23:137 (1962).

214. Sawicki, E., S.P. McPherson, T.W. Stanley, J. Meeker, and W.C. Elbert, Quantitative Composition of the Urban Atmosphere in Terms of Polynuclear Aza Heterocyclic Compounds and Aliphatic and Polynuclear Aromatic Hydrocarbons, Intern. J. Air Water Pollution 9:515 (1965).

215. Sawicki, E., T.W. Stanley, W.C. Elbert, J. Meeker, and S.P. McPherson, Comparison of Methods for the Determination of Benzo(a)pyrene in Particulates from Urban and Other Atmospheres, Atmos. Environ. 1:131 (1967).

216. Sawicki, E., T.W. Stanley, T.R. Hauser, H. Johnson, and W.C. Elbert, Correlation of Piperonal Test Values for Aromatic Compounds with the Atmospheric Concentration of Benzo(a)-pyrene, Intern. J. Air Water Pollution 7:57 (1963).

217. Sawicki, E., W.C. Elbert, R. Thomas, T.R. Hauser, F.T. Fox, and T.W. Stanley, Benzo(a)pyrene Content of the Air of American Communities, Am. Ind. Hyg. Assoc. J. 21:443 (1960).

218. Saxen, E., and Z. Schweiz, Report from Finnish Cancer Registry, Allgem. Bakteriol. 18:556 (1955).

219. Schrek, R., L.A. Baker, G.P. Ballard, and S. Kolgoff, Tobacco Smoking as an Etiologic Factor in Disease. I. Cancer, Cancer Res. 10:49 (1950).

220. Scurfield, G., Air Pollution and Tree Growth, Forestry Abstr. 21:339, 517 (1960).

221. Shahab, L.M., Vopr. Onkol. 3:387 (1957).

222. Shahab, L.M., Experimental Research on the Link Between Atmospheric Pollution and Lung Cancer, Intern. J. Air Pollution 3:221 (1960).

223. Shahab, L.M., Studies in the U.S.S.R. on the Distribution, Circulation, and Fate of Carcinogenic Hydrocarbons in the Human Environment and the Role of Their Deposition in Tissues in Carcinogenesis: A Review, Cancer Res. 27:1132 (1967).

224. Shahab, L.M., On the Distribution and Fate of the Carcinogenic Hydrocarbon Benz(a)pyrene (3,4 Benzpyrene) in the Soil, Z. Krebsforsch. 70:204 (1968).

225. Shahab, L.M., L.N. Pylev, and T.S. Kolesnichenko, Importance of Local Retention of Carcinogenic Agent in Pathogenesis of Lung Cancer (Experimental Investigation), Vopr. Onkol. 10(6): 65 (1964).

226. Shira, R.B., J. Oral Surg. 26:695 (1968).

227. Shubik, P., Biological Determination of the Action of Chemical Carcinogens, in Proceedings of the Fourth National Cancer Conference, (Philadelphia: Lippincott, p. 113 1961).

228. Shubik, P., et al., Studies on Promoting Action in Skin Carcinogenesis, Proc. Am. Assoc. Cancer Res. 2:146 (1956).

229. Simmers, M.H., Cancers in Mice From Asphalt Fractions, Ind. Med. Surg. 34:573 (1965).

230. Skramovsky, V., The Determination of 3,4-Benzpyrene in the Atmosphere of Prague, Acta Unio Intern. Contra Cancrum 19: 733 (1963).

231. Smith, W.S., Atmospheric Emissions from Fuel Oil Combustion, U.S. Public Health Serv. Publ. 999-AP-2 (1962).

232. Smoking and Health: Report of the Advisory Committee to the Surgeon General, U.S. Public Health Serv. Publ. 1103.

233. Stanley, T.W., J.E. Meeker, and M.J. Morgan, Extraction of Organics from Airborne Particulates, Environ. Sci. Tech. 1: 927 (1967).

234. Stanley, T.W., M.J. Morgan, and J.E. Meeker, Thin-Layer Chromatographic Separation and Spectrophotometric Determination of Benzo(a)pyrene in Organic Extracts of Airborne Particulates, Anal. Chem. 39:1327 (1967).

235. Stedman, R.L., The Chemical Composition of Tobacco and Tobacco Smoke, Chem. Rev. 68:153 (1968).

236. Steiner, P.E., The Conditional Biolgical Activity of the Carcinogens in Carbon Blacks and Its Elimination, Cancer Res. 14:103 (1954).

237. Steiner, P.E., and H.L. Falk, Summation and Inhibition Effects of Weak and Strong Carcinogenic Hydrocarbons: 1:2-Benzanthracene, 1:2:5:6-Dibenzanthracene and 20-Methylcholanthrene, Cancer Res. 11:56 (1951).

238. Stenburg, R.L., D.J. vonLehmden, and R.P. Hangebrauck, Sample Collection Techniques for Combustion Sources--Benzopyrene Determination, Am. Ind. Hyg. Assoc. J. 22:271 (1961).

239. Stevenson, J.L., and E. Von Haam, Carcinogenicity of Benz(a)-anthracene and Benzo(c)phenanthrene Derivatives, Am. Ind. Hyg. Assoc. J. 26:475 (1965).

240. Stewart, H., Pulmonary Cancer and Adenomatosis in Captive Wild Mammals and Birds from the Philadelphia Zoo, J. Natl. Cancer Inst. 36(1):117 (1966).

241. Stocks, P., in Studies on Medical Population Subjects, H.M. Stationery Office, London (1947).

242. Stocks, P., Endemiology of Cancer of the Lung in England and Wales, Brit. J. Cancer 6:99 (1952).

243. Stocks, P., Air Pollution and Cancer Mortality in Liverpool Hospital Region and North Wales, Intern. J. Air Pollution 1:1 (1958).

244. Stocks, P., in British Empire Campaign; Thirty-Fifth Annual Report Covering the Year 1957, Supplement to Part II, British Empire Cancer Campaign, London (1958).

245. Stocks, P., On the Relations Between Atmospheric Pollution in Urban and Rural Localities and Mortality from Cancer, Bronchitis, and Pneumonia, with Particular Reference to 3:4 Benzopyrene, Beryllium, Molybdenum, Vanadium, and Arsenic, Brit. J. Cancer 14:397 (1960).

246. Stocks, P., Recent Epidemiological Studies of Lung Cancer Mortality, Cigarette Smoking and Air Pollution, with Discussion of a New Hypothesis of Causation, Brit. J. Cancer 20:595 (1966).

247. Stocks, P., Lung Cancer and Bronchitis in Relation to Cigarette Smoking and Fuel Consumption in 20 Countries, Brit. J. Prevent. Social Med. 21:181 (1967).

248. Stocks, P., and J.M. Campbell, Lung Cancer Death Rates Among Non-Smokers and Pipe and Cigarette Smokers, Brit. Med. J. 2:923 (1955).

249. Stocks, P., B.T. Commins, and K.V. Aubrey, A Study of Polycyclic Hydrocarbons and Trace Elements in Smoke in Merseyside and Other Northern Localities, Intern. J. Air Water Pollution 4:141 (1961).

250. Stokinger, H.E., and D.L. Coffin, "Biological Effects of Air Pollutants," in Air Pollution, vol. I (New York: Academic Press, 1968).

251. Sullivan, J.L., and G.J. Cleary, A Comparison of Polycyclic Aromatic Hydrocarbon Emissions from Diesel- and Petrol-Powered Vehicles in Partially Segregated Traffic Lanes, Brit. J. Ind. Med. 21:117 (1964).

252. Swann, H.E., and O.J. Balchum, Biological Effects of Urban Air Pollution. IV. Effects of Acute Smog Episodes on Respiration of Guinea Pigs, Arch. Environ. Health 12:698 (1966).

253. Swann, H.E., D. Brunol, L.G. Wayne, and O.J. Balchum, Biological Effects of Urban Air Pollution. II. Chronic Exposure of Guinea Pigs, Arch. Environ. Health 11(6):765 (1965).

254. Tanimura, H., Benzo(a)pyrene in an Iron and Steel Works, Arch. Environ. Health 17:172 (1968).

255. Thomas, M.D., Air Pollution with Relation to Agronomic Crops. I. General Status of Research on Effects of Air Pollution on Plants, Agron. J. 50:545 (1958).

256. Thomas, M.D., "Effects of Air Pollution on Plants," in Air Pollution, World Health Organ. Monograph Ser. 46 (New York: Columbia Univ. Press, pp. 233-278, 1961).

257. Thomas, M.D., and R.H. Hendricks, "Effect of Air Pollutants on Plants," in Air Pollution Handbook, P.O. Magill, F.R. Holden, and C. Ackley, Eds. (New York:McGraw-Hill, 1956).

258. Threshold Limit Values for 1967--Recommended and Intended Values, 29th Annual Meeting of the American Conference of Governmental Industrial Hygienists, Chicago, Ill. (May 1-2, 1967).

259. Tipson, R.S., A. Cohen, and A.J. Fatiadi, Air Pollution Studies, Natl. Bur. Std. Technical Note 427, p. 11 (Oct. 1967).

260. Tomingas, R., Soot Hazards Investigated from Their Carcinogenic Aspects, Staub-Reinhalt, Luft 27(8):8 (1967).

261. Toth, B., and P. Shubik, Carcinogenesis in AKR Mice Injected at Birth with Bezo(a)pyrene and Dimethylnitrosamine, Cancer Res. 27(1):43 (1967).

262. Troll, W., The Role of Analytical Chemistry in Carcinogenesis Studies, Anal. Chem. 41:22A (1969).

263. Tye, R., and K.L. Stemmer, Experimental Carcinogenesis of the Lung. II. Influence of Phenols in the Production of Carcinoma, J. Natl. Cancer Inst. 39:175 (1967).

264. Tye, R., A.W. Horton, and I. Rapien, Benzo(a)pyrene and Other Aromatic Hydrocarbons Extractable from Bituminous Coal, Am. Ind. Hyg. Assoc. J. 27:25 (1966).

265. Tye, R., M.J. Burton, E. Bingham, Z. Bell, and A.W. Horton, Carcinogens in a Cracked Petroleum Residuum. The Contributions of Various Polycyclic Aromatic Hydrocarbons to the Carcinogenic Potency of a Catalytically Cracked Oil, Arch. Environ. Health 13:202 (1966).

266. Valori, P., C. Melchiorri, and N. Vescia, Detection and Determination of Polynuclear Hydrocarbons in the Atmospheric Dust of the City of Rome. I. Determination of 3,4-Benzpyrene, Nuovi Ann. Ig. Microbiol. 14:434 (1963).

267. Valori, P. *et al*., Carcinogenic Contaminates in the Atmosphere. Determination of the Polycyclic Aromatic Hydrocarbons in the Atmosphere of Rome, Nuovi Ann. Ig. Microbiol. 17:264 (1967).

268. VanDuuren, B.L., L. Orris, and N. Nelson, Carcinogenicity of Epoxides, Lactones, and Peroxy Compounds. II, J. Natl. Cancer Inst. 35:707 (1965).

269. VanDuuren, B.L. *et al*., Carcinogenicity of Epoxides, Lactones, and Peroxy Compounds, J. Natl. Cancer Inst. 31:41 (1963).

270. vonLehmden, D.J., R.P. Hangebrauck, and J.E. Meeker, Polynuclear Hydrocarbon Emissions from Selected Industrial Processes, J. Air Pollution Control Assoc. 15:306 (1965).

271. Waller, R.E., The Benzpyrene Content of Town Air, Brit. J. Cancer 6:8 (1952).

272. Waller, R.E., and B.T. Commins, Studies of the Smoke and Polycyclic Aromatic Hydrocarbon Content of the Air in Large Urban Areas, Environ Res. 1:295 (1967).

273. Waller, R.E., B.T. Commins, and P.J. Lawther, Air Pollution in a City Street, Brit. J. Ind. Med. 22:128 (1965).

274. Ward, B., Sir Edwin Chadwick, National Health, (London: Richardson, Longmans Green, p.311, 1890); quoted by A. Wolman, Science 159:1437 (1968).

275. Weisburger, J.H., and E.K. Weisburger, Chemicals as Causes of Cancer, Chem. Eng. News, 44:124 (Feb. 7, 1966).

276. Wettig, K., Essay on the Problematics Concerning the Determation of Benzpyrene in Atmospheric Air, Neoplasma 14:181 (1967).

277. White, R.H., and J.W. Howard, Thin-Layer Chromatography of Polycyclic Aromatic Hydrocarbons, J. Chromatog. 29:108 (1967).

278. Willis, R.A., Pathology of Tumors, 3rd ed. (London: Butterworths, 1960).

279. Wilmhurst, J.R., Gas Chromatographic Analysis of Polynuclear Arenes, J. Chromatog. 17:50 (1965).

280. Winkelstein, Jr., W., and S. Kantor, Stomach Cancer, Arch. Environ. Health 18:544 (1969).

281. Wiseley, D.W., P. Kotin, P.R. Fowler, and J. Trivedi, The Combined Effect of Repeated Viral Infection and Exposure to Carcinogenic Aerosols on Pulmonary Tumor Induction in C57 Black Mice, Proc. Am. Assoc. Cancer Res. 3:278 (1961).

282. Won, W.D., and J.F. Thomas, Developmental Work on Bioassay Technique for Atmospheric Pollutants, Natl. Cancer Inst. Monograph No. 9, p. 59 (1962).

283. World Health Organ., Tech. Rept. Ser. 220 (1961).

284. Wynder, E.L., and E.A. Graham, Tobacco Smoking as a Possible Etiologic Factor in Bronchiogenic Carcinoma. A Study of 684 Proned Cases, J. Am. Med. Assoc. 143:329 (1950).

285. Wynder, E.L., and E.C. Hammond, A Study of Air Pollution Carcinogenesis, Cancer 15:79 (1962).

286. Wynder, E.L., and D. Hoffmann, A Study of Air Pollution Carcinogenesis. II. Carcinogenic Activity of Gasoline Engine Exhaust Condensate, Cancer 15:103 (1962).

287. Wynder, E.L., and D. Hoffmann, Tobacco and Tobacco Smoke, (New York: Academic Press, 1967).

288. Wynder, E.L., and D. Hoffmann, Experimental Tobacco Carcinogenesis, Science 162:862 (1968).

289. Wynder, E.L., I.J. Bross, and E. Day, Study of Environmental Factors in Cancer of Larynx, Cancer 9:86 (1956).

290. Yanysheva, N.Ya., I.S. Kireeva, and N.N. Serzhantova, Hyg. Sanitation 28:71 (1963).

291. Yanysheva, N.Ya., I.S. Kireeva, and N.N. Serzhantova, The Problem of Removing the Carcinogenic Properties of Brick Coal, Gigiena i Sanit. 29:10 (1964).

292. Yanysheva, N.Ya., L.C. Andrienko, N.V. Balenko, and I.S. Kireeva, Removal of Carcinogens from Coal Briquets, Hyg. Sanitation 29:6 (1964).

293. Zanetti, M., and F. Cutrufelli, The 3,4-Benzpyrene in Urban and Extra-urban Atmosphere of Bologna, Nuovi Ann. Ig. Microbiol. 12:100 (1961).

294. Zeidberg, L.D., R.A. Prindle, and E. Landau, The Nashville Air Pollution Study. III. Morbidity in Relation to Air Pollution. Am. J. Pub. Health 54:85 (Jan. 1964).

295. Zeidberg, L. D., R. M. Hagstrom, H. A. Sprague, and E. Landau, Nashville Air Pollution Study. VII. Mortality from Cancer in Relation to Air Pollution, Arch. Environ. Health 15:237 (1967).

296. Zeidberg, L. D., R. J. M. Horton, and E. Landau, The Nashville Air Pollution Study. V. Mortality from diseases of the Respiratory System in Relation to Air Pollution, Arch. Environ. Health 15:214 (1967).

APPENDIX

APPENDIX

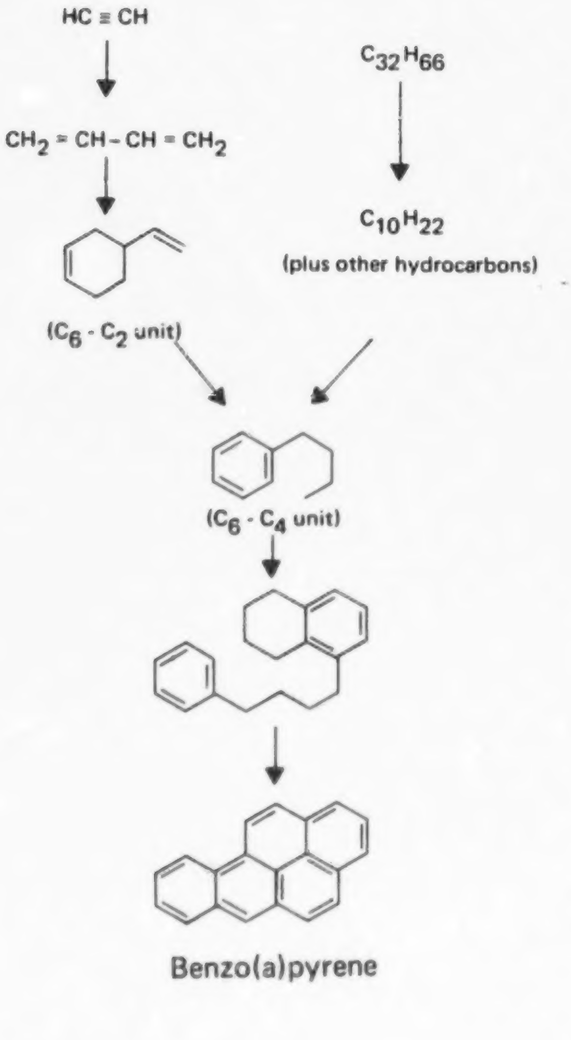

HC ≡ CH
CH2 = CH - CH = CH2
(C6 - C2 unit)
C32H66
C10H22
(plus other hydrocarbons)
(C6 - C4 unit)
Benzo(a)pyrene

FIGURE 2

Benzo(a)pyrene Pyrosynthesis (as Suggested by Badger)[103]

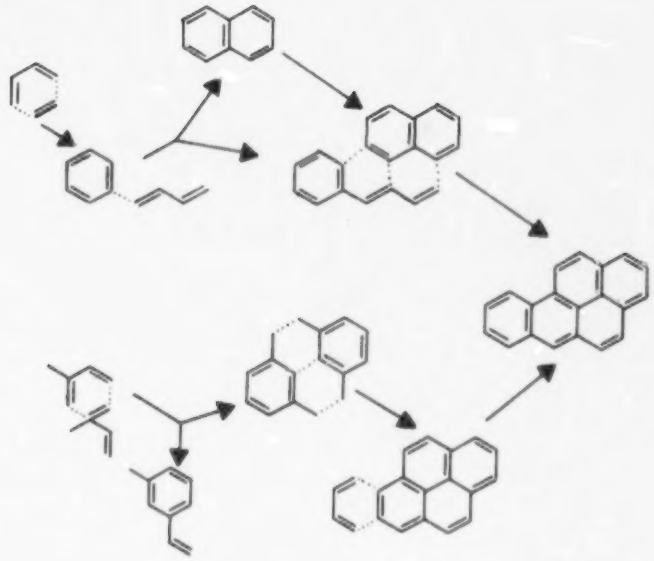
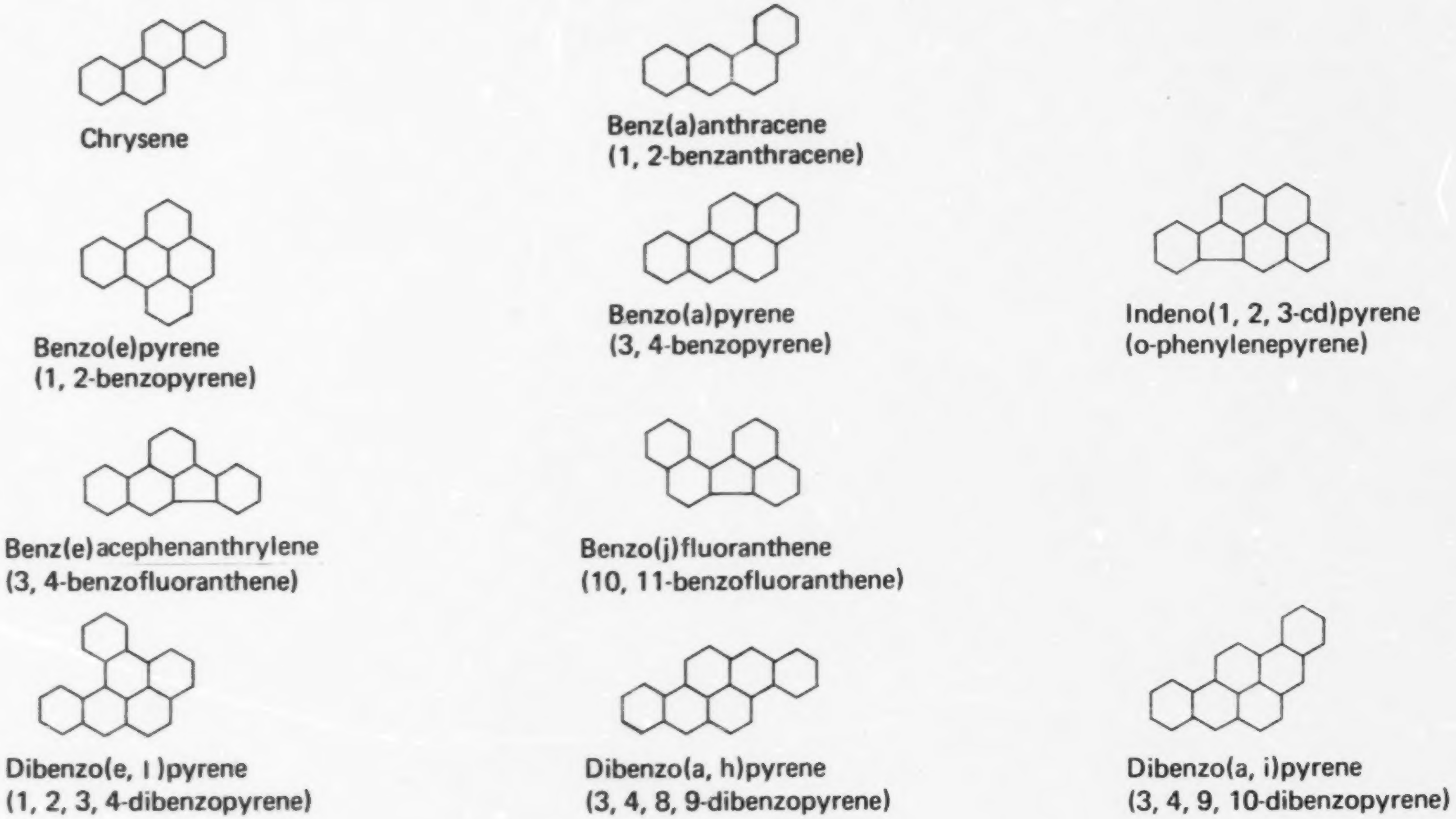


FIGURE 3

Pathways for the Pyrosynthesis of Benzo(a)pyrene[103]



Chrysene

Benz(a)anthracene
(1, 2-benzanthracene)

Benzo(e)pyrene
(1, 2-benzopyrene)

Benzo(a)pyrene
(3, 4-benzopyrene)

Indeno(1, 2, 3-cd)pyrene
(o-phenylenepyrene)

Benz(e)acephenanthrylene
(3, 4-benzofluoranthene)

Benzo(j)fluoranthene
(10, 11-benzofluoranthene)

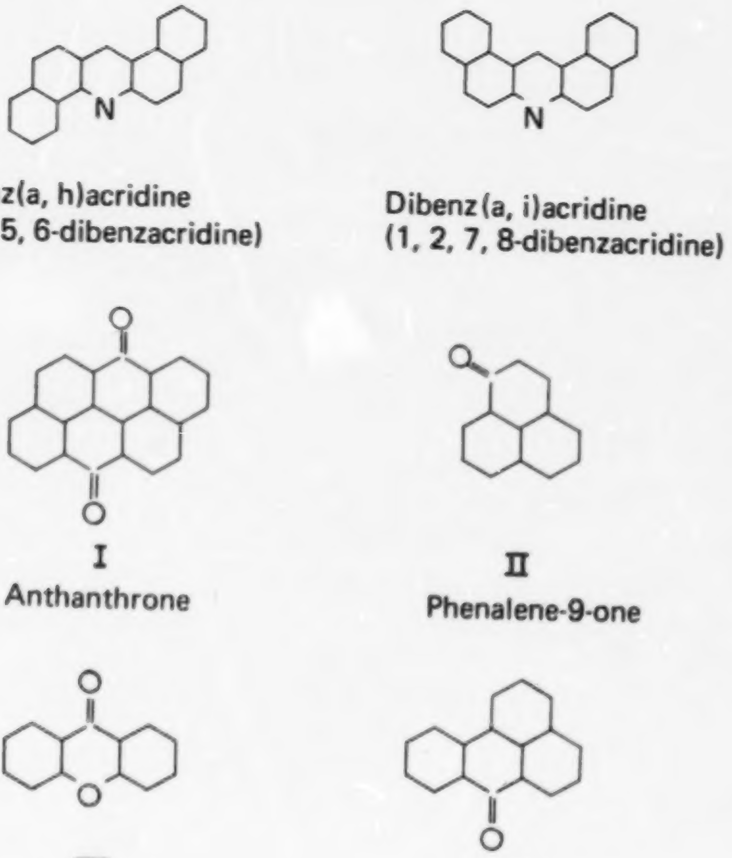
Dibenzo(e, l)pyrene
(1, 2, 3, 4-dibenzopyrene)

Dibenzo(a, h)pyrene
(3, 4, 8, 9-dibenzopyrene)

Dibenzo(a, i)pyrene
(3, 4, 9, 10-dibenzopyrene)

FIGURE 4

Carcinogenic Polynuclear Aromatic Hydrocarbons
Identified in Urban Air[103]



Dibenz(a, h)acridine
(1, 2, 5, 6-dibenzacridine)

Dibenz(a, i)acridine
(1, 2, 7, 8-dibenzacridine)

I
Anthanthrone

II
Phenalene-9-one

III
Xanthene-9-one

IV
7H-benz(de)anthracen-7-one

FIGURE 5

Aza-Heterocyclics and Polynuclear Carbonyl Compounds Identified in Urban Air[103]

APPENDIX

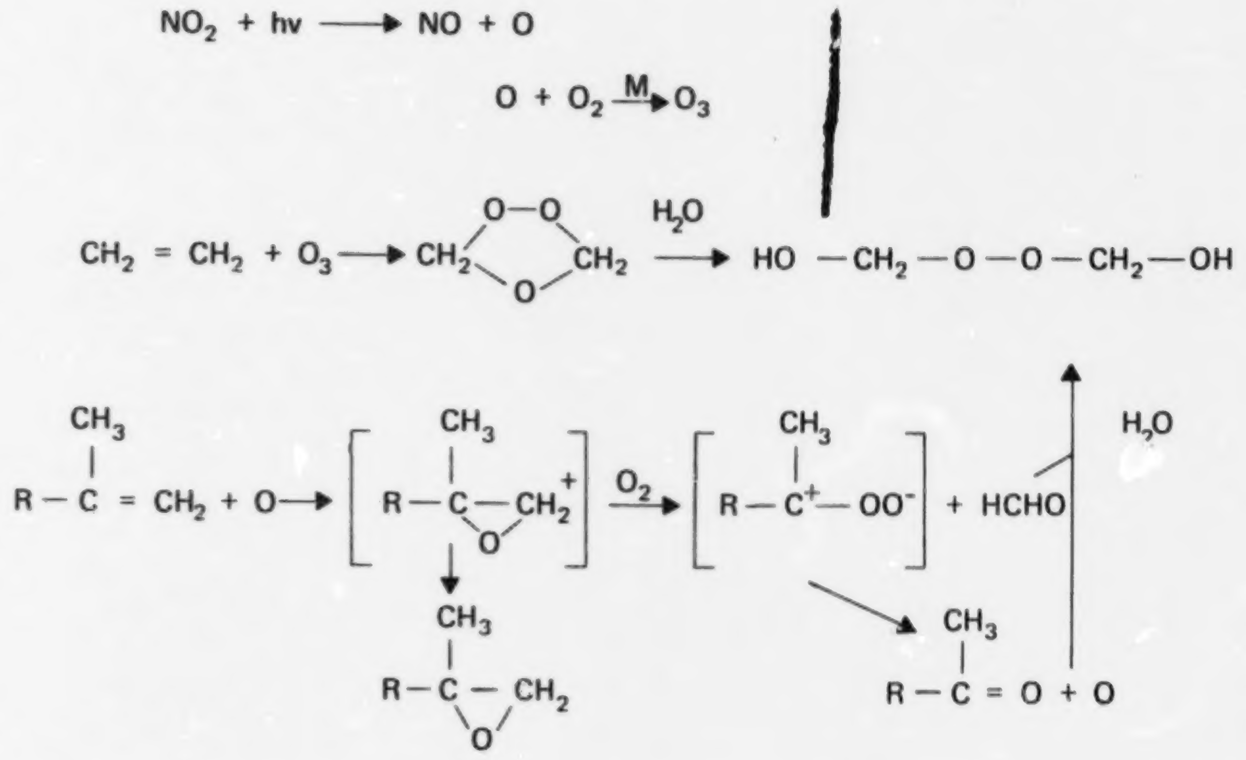


FIGURE 6

Reaction Pattern Showing the Products of Decomposition of Unsaturated Hydrocarbons. Identification Accomplished by Infrared Spectroscopy and Gas Chromatography.[186]

TABLE 4

TUMOR INDUCTION IN MICE FOLLOWING CUTANEOUS ADMINISTRATION OF ORGANIC EXTRACTS OF PARTICULATE ATMOSPHERIC POLLUTANTS[64]

Particulates	Extract	Administration	Latent Period (months)	% Tumor Yield		Comments
				Local	Distant	
Filtration and precipitation	Benzene-ether	Subcutaneous x 1 (~50,000 ug)	12	6		Particulates from 5 urban sites
Large capacity collectors	Benzene	Subcutaneous x 1 (~50,000 ug)	16	8		Similar tumor yields from samples of 5 urban sites
Filtration and sedimentation	Dichloroethane	Painting 3 x wkly (10% benzene sol.)	6	38	Multiple Adenomas	Particulates from 3 urban sites
Large volume collectors	Benzene	Painting 3 x wkly (acetone sol.)	15	42		Particulates from Los Angeles
Ventilation filters	Benzene and 2 fractions	Painting 3 x wkly (1% benzene sol.)	?	45	Multiple Adenomas 16	Particulates from Liverpool, England
Oxidation products of aliphatics	Benzene	Painting 3 x wkly (acetone sol.)	14	20		Aromatic-free aerosol collected in Shepherd traps
Filtration of city smoke	Benzene	Painting 6 x only (1% benzene sol.)	18	20		Particulates from Newcastle, England

(continued)

TABLE 4 (Continued)

TUMOR INDUCTION IN MICE FOLLOWING CUTANEOUS ADMINISTRATION OF ORGANIC EXTRACTS OF PARTICULATE ATMOSPHERIC POLLUTANTS

Particulates	Extract	Administration	Latent Period (months)	% Tumor Yield		Comments
				Local	Distant	
Composite NASN samples	Benzene and 3 fractions	Subcutaneous x 24 (organic ~130,000 μg) (aromatic ~13,000-33,000 μg) (oxygenated ~12,000 μg) (aliphatic ~24,000 μg); Painting 2 x wkly (aliphatic and oxygenated)	9-26	2-10		Different tumor yields from samples of 8 urban sites. In general, low tumor yields obtained
Composite NASN, camp, samples	Benzene	Subcutaneous x 3 to neonates (15,000-25,000 μg)	3-12	1	Hepatomas, 8-83; Lymphomas, 1-17; Multiple adenomas, 13-75	Different tumor yields from samples of 6 urban sites. Results suggest role of several carcinogens

TABLE 5

TUMOR INCIDENCE FOLLOWING INJECTION OF ORGANIC ATMOSPHERIC POLLUTANTS TO NEONATAL MICE[64]

		Groups				% Tumor Incidence[a]			
Series	Dose (μg) of Organic Pollutants	No. Neonates Injected	Sex	No. at Weaning	No. at Risk[b]	Pulmonary, Solitary	Adenomas, Multiple	Hepatomas	Lymphoma
Uninjected controls	0	90	M	36	30	13	0	7	0
			F	37	36	3	0	0	0
Solvent controls	0	100	M	47	44	11	0	2	0
			F	42	39	8	0	0	0
Chicago '63 (10024)	25,000	117	M	42	22	27	50	14	5
			F	37	37	19	19	0	8
Cincinnati '63 (10025)	25,000	123	M	32	16	25	63	31	6
			F	31	27	11	74	4	15
Los Angeles '63 (10026)	25,000	77	M	27	11	36	27	9	18
			F	22	21	5	10	0	5

[a] Tests terminated at each 50 weeks.

[b] Excluding deaths <50 weeks from unrelated causes, notably obstructive renal failure in males, also losses due to cannibalism or autolysis.

TABLE 6

ESTIMATED ANNUAL BENZO(A)PYRENE (BAP) EMISSIONS FOR THE UNITED STATES[91]

Source	Estimated BaP Emission Rate	Estimated Annual Consumption or Production	Estimated Annual BaP Emission (tons)
Heat generation	($\mu g/10^6$ Btu)	(10^{15} Btu)	
Coal			
Residential			
(i) hand-stoked	1,400,000	0.26	400
(ii) underfeed	44,000	0.20	9.7
Commercial	5,000	0.51	2.8
Industrial	2,700	1.95	5.8
Electric generation	90	6.19	0.6
Oil	200	6.79	1.5
Gas	100	10.57	1.2
Total			421.6
Refuse burning	(μg/ton)	(10^6 tons)	
Incineration			
Municipal	5,300	18	0.1
Commercial	310,000	14	4.8
Open burning			
Municipal refuse	310,000	14	4.8
Grass, leaves	310,000	14	4.8
Auto components	26,000,000	0.20	5.7
Total			20.2

(continued)

TABLE 6 (Continued)

ESTIMATED ANNUAL BENZO(A)PYRENE (BAP) EMISSIONS FOR THE UNITED STATES

Source	Estimated BaP Emission Rate	Estimated Annual Consumption or Production	Estimated Annual BaP Emission (tons)
Industries	(µg/bl)	(10^6 bl)	
Petroleum catalytic			
Cracking (catalyst regeneration)			
FCC[a]			
(i) no Co boiler[b]	240	790	0.21
(ii) with CO boiler	14	790	0.012
HCC[c]			
(i) no CO boiler	218,000	23.3	5.6
(ii) with CO boiler	45	43.3	0.0024
TCC[d] (air lift)	(µg/bl)	(10^6 bl)	
(i) no CO boiler	90,000	131	13.0
(ii) with CO boiler	<45	59	<0.0029
CC (bucket lift)			
(i) no CO boiler		119	0.0041
(ii) with CO boiler	<31	0	0
Asphalt road mix	50 µg/ton	187,000 tons	0.000010
Asphalt air blowing	<10,000 µg/ton	4,400 tons	<0.000048
Carbon-black manufacturing	Atmospheric samples indicate that BaP Emissions from these processes are not extremely high		
Steel & Coke manufacturing			
Chemical complex			
Total			18.8

(continued)

TABLE 6 (Continued)

ESTIMATED ANNUAL BENZO(A)PYRENE (BAP) EMISSIONS FOR THE UNITED STATES

Source	Estimated BaP Emission Rate	Estimated Annual Consumption or Production	Estimated Annual BaP Emission (tons)
Motor vehicles	(μg/gal)	(10^{10} gal)	
Gasoline			
Automobiles	170	4.61	8.6
Trucks	>460	2.01	>10
Diesel	690	0.257	2.0
Total			>20.6
Total (all sources tested)			481

[a] FCC: fluid catalytic cracker.

[b] CO boiler: carbon monoxide waste heat boiler.

[c] HCC: Houdriflow catalytic cracker.

[d] TCC: Thermo for catalytic cracker.

TABLE 7

BENZO(A)PYRENE CONCENTRATIONS IN URBAN SAMPLING SITES FOR JANUARY THROUGH MARCH 1959[119,217]

State	City	µg BaP/g of Particulate	µg BaP of Benzene Soluble Fraction	µg BaP/ m^3 air
Alabama	Montgomery	340	2,000	.024
Alaska	Anchorage	64	540	.0038
Arizona	Phoenix	15	160	.0050
Arkansas	Little Rock	20	230	.0015
California	Berkeley	41	260	.0029
	Glendale	5.3	38	.0008
	San Bernardino	13	140	.0023
	San Diego	20	150	.0021
	San Jose	7.2	91	.00056
Colorado	Denver	51	290	.0069
Connecticut	Hartford	68	730	.0065
	New Britain	50	450	.0055
	New Haven	53	580	.0053
Delaware	Wilmington	55	650	.010
District of Columbia	Washington	71	59	.0093
Florida	Miami	28	250	.0019
	Orlando	110	810	.011
	Tampa	140	1,200	.015
Georgia	Savannah	49	480	.0043
Illinois	Chicago	74	950	.015
	Rockford	63	660	.0073
Indiana	East Chicago[a]	34	710	.0111
	Indianapolis	120	1,100	.026
	Hammond	280	2,600	.039
	South Bend	91	200	.016
Iowa	Des Moines	160	1,600	.023
Kansas	Topeka	40	510	.0031
	Wichita	19	310	.0023
Kentucky	Louisville	70	860	.016
Louisiana	Shreveport	6.4	150	.00065
Maine	Portland	180	2,100	.021
Maryland	Baltimore	64	650	.014
Massachusetts	Boston	45	730	.0096
	Lowell	40	410	.0031
	New Bedford	81	1,000	.0044
	Worcester	66	700	.014
Michigan	Dearborn	110	960	.0090
	Flint	140	1,400	.015
	Grand Rapids	91	1,400	.015

(continued)

TABLE 7 (Continued)

BENZO(A)PYRENE CONCENTRATIONS IN URBAN
SAMPLING SITES FOR JANUARY THROUGH MARCH 1959

State	City	of Particulate	μg BaP/g of Benzene Soluble Fraction	μg BaP/ m^3 air
Minnesota	Duluth[b]	110	1,500	.012
	Minneapolis	73	1,600	.014
Mississippi	Jackson	24	230	.0012
Missouri	Kansas City	46	540	.0065
	St. Louis	200	1,800	.054
Montana	Helena	2.4	51	.00011
Nebraska	Omaha	33	460	.0035
Nevada	Las Vegas	16	160	.0014
New Hampshire	Manchester	53	600	.0060
New Jersey	Bayonne	33	410	.0055
	Jersey City	33	440	.0060
	Newark	46	500	.0045
	Paterson	51	610	.0063
New Mexico	Albuquerque	15	460	.0063
North Carolina	Charlotte	290	2,100	.039
	Raleigh	180	1,300	.014
North Dakota	Bismarck	5.8	130	.00044
Ohio	Cleveland	110	1,200	.024
	Columbus	70	930	.0095
	Dayton	78	760	.0079
	Hamilton	83	600	.014
	Toledo	100	1,200	.011
	Youngstown	190	2,000	.028
Oklahoma	Tulsa	13	180	.0010
Oregon	Portland	96	730	.0080
Pennsylvania	Allentown	26	440	.0034
	Altoona[a]	280	1,400	.061
	Erie	70	1,000	.0095
	Johnstown	58	660	.016
	Pittsburgh	16	200	.0051
	Scranton	33	360	.0061
	York	31	510	.0056
Rhode Island	Providence	24	240	.0029
South Carolina	Charleston	68	530	.0056
	Columbia[a]	120	750	.024
South Dakota	Sioux Falls	31	480	.0040
Tennessee	Chattanooga	120	1,000	.031
	Knoxville	210	1,900	.024
Texas	Beaumont	13	200	.00082
	Dallas	6.1	160	.0014
	Galveston	3.4	50	.00016
	Houston	12	210	.0016
	San Antonio	5.8	110	.00086

(continued)

TABLE 7 (Continued)

BENZO(A)PYRENE CONCENTRATIONS IN URBAN SAMPLING SITES FOR JANUARY THROUGH MARCH 1959

State	City	μg BaP/g of Particulate	μg BaP/g of Benzene Soluble Fraction	μg Bap/ m^3 air
Utah	Salt Lake City	5.4	54	.00052
Vermont	Burlington	28	39	.0010
Virginia	Norfolk	59	580	.0084
	Richmond	410	1,900	.045
	Roanoke	160	1,100	.018
Washington	Seattle	81	790	.0090
West Virginia	Charleston[a]	40	900	.014
	Wheeling	140	1,600	.021
Wisconsin	Madison	80	830	.0049
	Milwaukee	60	730	.0085
Wyoming	Cheyenne	36	340	.0012

[a] In respect to the cities with benzo(a)pyrene levels greater than 11 μg/1,000 m^3 of air, five cities had a concentration of particulates in the air 1.5 to 2 times higher than in the corresponding January to March period in 1958.

[b] The concentration of particulates in the air for this city in January to March 1959 was half that found in the corresponding period of 1958.

TABLE 8

POLYNUCLEAR HYDROCARBON CONTENT OF PARTICULATE MATTER FOR SELECTED CITIES[213]

City	Month	Compound*								Total
		BghiP*	BaP	BeP	BkF	P	Cor	Per	Anth	
Winter 1959 (μg/g benzene soluble fraction)										
Atlanta	Feb.	830	690	440	560	560	400	100	48	3628
Birmingham	Feb.	1090	1500	610	800	1000	210	330	130	5670
Detroit	Feb.	2100	2000	1500	1300	1600	410	390	130	9430
Los Angeles	Feb.	510	150	230	160	170	330	44	4.5	1599
Nashville	Jan.	880	1300	710	790	1400	240	230	92	5642
New Orleans	Feb.	760	430	670	410	240	280	84	11	2885
San Francisco	Jan.	590	180	230	130	150	380	27	8.1	1695
Seattle	Jan.-Mar.	1200	790	--	710	590	1300	210	91	4891
Sioux Falls	Jan.-Mar.	1000	480	--	330	480	440	99	27	2856
South Bend	Jan.-Mar.	1500	2000	1700	1300	3900	480	370	190	11440
Wheeling	Jan.-Mar.	1100	1600	--	990	1700	360	200	110	6060
Youngstown	Jan.-Mar.	1600	2000	--	1300	2400	240	530	240	8310
Summer 1958 (μg/g benzene soluble fraction)										
Atlanta	July	510	160	150	130	73	250	40	20	1333
Birmingham	July	950	730	670	520	240	270	240	29	3649
Cincinnati	July	600	390	400	350	170	280	93	6.5	2290
Detroit	July	1500	950	840	770	440	290	270	61	5121
Los Angeles	July	200	43	54	39	23	190	29	2.4	580.4
Nashville	July	440	180	150	130	75	160	27	7.7	1170
New Orleans	July	530	230	360	210	39	290	45	12	1716
Philadelphia	July	960	480	350	350	310	410	110	17	2987
San Francisco	July	720	69	150	67	25	450	12	6.1	1499

*BghiP = Benzolg, h, ilperylene; BaP = Benzo(a)pyrene; BeP = Benzo(e)pyrene; BkF = Benzo(k)fluoranthene; P = Pyrene; Cor = Coronene; Per = Perylene; Anth = Anthanthrene

TABLE 9

SEASONAL EFFECT ON THE BENZO(A)PYRENE CONCENTRATIONS OF VARIOUS URBAN ATMOSPHERES[39]

Location	Year	Concentrations ($\mu g/m^3$ of air)	
		Summer (low)	Winter (high)
Atlanta, Ga.	1958	0.0016	0.015
	1960	0.0009	0.014
Birmingham, Ala.	1958	0.006	0.074
	1960	0.003	0.062
Cincinnati, Ohio	1958	0.002	0.026
	1960	0.0012	0.018
Detroit, Mich.	1958	0.0034	0.031
Location I	1961	0.0072	0.017
Location II	1961	0.0036	0.0137
Location III	1963	0.0002	0.0018
Los Angeles, Calif.	1958	0.0004	0.013
Nashville, Tenn.	1958	0.0014	0.055
New Orleans, La.	1958	0.0020	0.006
	1960	0.0006	0.007
New York, N.Y.			
Herald Square	1963-64	0.0005	0.0094
Columbus Circle	1964	0.0007	0.0026
Philadelphia, Pa.	1958	0.0025	0.019
San Francisco, Calif.	1958	0.0003	0.0075
South Charleston, W. Va.	1960	0.0006	0.012

TABLE 10

CONCENTRATIONS OF BENZO(A)PYRENE IN THE AMBIENT AIR, 1966[4]
($\mu g/m^3$)

Location	1st Quar.	2nd Quar.	3rd Quar.	4th Quar	Yearly Avg
Alabama					
Birmingham	.0163	.0163	.00536	.036	.01849
Gadsden	.00297	.00297	.00176	.00626	.00349
Mobile	.00239	.00239	.00671	.01430	.00645
Alaska					
Anchorage	.00392	.00392	.00063	.00063	.00228
Arizona					
Grand Canyon National Park*	.00028	.00028	.00036	.00022	.00029
Paradise Valley	.00000	.00000	.00104	.00023	.00032
Phoenix	.00135	.00135	.00266	.00140	.00169
Tucson	.0005	.0005	.00041	.00095	.00059
Arkansas					
Little Rock	.00072	.00072	.00126	.00198	.00117
Montgomery County*	.00036	.00036	.00012	.00042	.00032
Texarkana	.00027	.00027	.00086		
West Memphis	.0009	.0009	.00054	.00207	.0011
California					
Burbank	.00211	.00211	.0005	.00513	.00246
Humboldt County*	.00026	.00026	.00032	.00056	.00035
Los Angeles	.0024	.0024	.00086	.00257	.00206
Oakland	.00306	.00306	.00122	.00356	.00273
Pasadena	.00171	.00171	.0005	.00339	.00183
San Diego	.00117	.00117	.00041	.0041	.00171
San Francisco	.00108	.00108	.00095	.00122	.00108
Colorado					
Denver	.00104	.00104	.00225	.00486	.00230
Montezuma County*	.00006	.00006	.00010	.00006	.00007
Connecticut					
Hartford	.00248	.00248	.00135	.0027	.00225
New Haven	.00324	.00324	.00239	.00504	.00348
Delaware					
Kent County*	.00074	.00074	.00046	.00038	.00058
Newark	.00072	.00072	.00135	.00108	.00097
Wilmington	.00162	.00162	.00158	.00378	.00215

(continued)

TABLE 10 (Continued)

CONCENTRATIONS OF BENZO(A)PYRENE IN THE AMBIENT AIR, 1966
($\mu g/m^3$)

Location	1st Quar.	2nd Quar.	3rd Quar.	4th Quar.	Yearly Avg
District of Columbia					
Washington	.00090	.00090	.00068	.00693	.00235
Georgia					
Atlanta	.00113	.00113	.00144	.00185	.00139
Hawaii					
Honolulu	.00009	.00009	.00023	.00023	.00016
Idaho					
Boise	.00266	.00266	.00167	.00680	.00345
Butte County*	.00010	.00010	.00010		
Illinois					
Chicago	.00266	.00266	.00306	.00495	.00333
Indiana					
East Chicago	.00752	.00752	.00707	.005	.00678
Hammond	.00572	.00572	.00248	.00149	.00385
Indianapolis	.011	.011	.00707	.0124	.01037
Monroe State Forest*	.00044	.00044	.00048	.00050	.00047
Muncie	.00207	.00207	.00257	.00275	.00237
New Albany	.00293	.00293	.00099	.0147	.00539
Parke County*	.00134	.00134	.00026	.00054	.00087
South Bend	.00117	.00117	.00284	.00378	.00224
Terre Haute	.00689	.00689	.00806		
Iowa					
Davenport	.00509	.00509	.00158	.00095	.00318
Delaware County*	.00074	.00074		.00018	
Des Moines	.00279	.00279	.00216	.00243	.00254
Dubuque	.00509	.00509	.00171	.00225	.00354
Kansas					
Kansas City	.00108	.00108	.00149	.00108	.00118
Wichita	.00068	.00068	.00032	.00144	.00078
Kentucky					
Ashland	.0122	.0122	.00657	.0109	.01047
Covington	.00288	.00288	.00225	.00432	.00308
Louisville	.00257	.00257	.00167	.00324	.00251

(continued)

TABLE 10 (Continued)

CONCENTRATIONS OF BENZO(A)PYRENE IN THE AMBIENT AIR, 1966
(μg/m³)

Location	1st Quar.	2nd Quar.	3rd Quar.	4th Quar.	Yearly Avg
Louisiana					
New Orleans	.00203	.00203	.00158	.00347	.00228
Maine					
Acadia National Park*	.00012	.00012	.0004	.00008	.00018
Portland	.00180	.00180	.00171	.00177	.00177
Maryland					
Baltimore	.0023	.0023	.00171	.00473	.00276
Calvert County*	.001	.001	.00024	.00022	.00062
Michigan					
Detroit	.00459	.00459	.0027	.00702	.00473
Minnesota					
Duluth	.00149	.00149	.00396	.00198	.00223
Minneapolis	.00108	.00108	.00099	.00342	.00164
Moorhead	.00045	.00045	.00063	.0014	.00073
St. Paul	.00176	.00176	.00126	.00243	.00180
Mississippi					
Jackson	.00086	.00086	.00099	.00239	.00128
Jackson County*	.0002	.0002	.00006	.00014	.00015
Missouri					
Kansas City	.00234	.00234	.00122	.00108	.00175
St. Louis	.00698	.00698	.00167	.00563	.00532
Shannon County*	.00008	.00008	.00004	.00008	.00007
Montana					
Helena	.00234	.00234	.00018	.00077	.00141
Glacier National Park*	.00024	.00024	.00046	.00028	.00031
Nebraska					
Omaha	.00392	.00392	.00131	.00167	.00271
Thomas County*	.00012	.00012	.00008	.00026	.00015
Nevada					
Las Vegas	.00099	.00099	.00041	.00266	.00126
White Pine County*	.00004	.00004	.00002	.00008	.00005

(continued)

TABLE 10 (Continued)

CONCENTRATIONS OF BENZO(A)PYRENE IN THE AMBIENT AIR, 1966
($\mu g/m^3$)

Location	1st Quar.	2nd Quar.	3rd Quar.	4th Quar.	Yearly Avg
New Hampshire					
Concord	.00054	.00054	.00041	.00077	.00057
Coos County*	.00024	.00024	.00016	.00028	.00023
New Jersey					
Camden	.0027	.0027	.00207	.00441	.00297
Glassboro	.00081	.00081	.00018	.00113	.00073
Jersey City	.00509	.00509	.0023	.00419	.00417
Marlton	.0014	.0014	.00117	.00095	.00123
Newark	.00225	.00225	.00054	.0032	.00206
Perth Amboy	.00189	.00189	.00189	.00266	.00208
Trenton	.00216	.00216	.00063	.00369	.00216
New Mexico					
Albuquerque	.0023	.0023	.00036	.00311	.00202
Rio Arriba County*	.00018	.00018	.0001	.00028	.00019
New York					
New York City	.00491	.00491	.00158	.005	.0041
Cape Vincent*	.0002	.0002	.00032	.00016	.00022
North Carolina					
Charlotte	.00509	.00509	.00077	.0119	.00571
Cape Hatteras*	.00016	.00016	.00018	.00038	.00022
Ohio					
Akron	.00468	.00468	.00153	.00545	.00409
Cincinnati	.00432	.00432	.00113	.00441	.00355
Cleveland	.00356	.00356	.00207	.00338	.00314
Columbus	.00405	.00405	.00162	.00194	.00292
Dayton	.00275	.00275	.00203	.00329	.00271
Toledo	.00221	.00221	.0009	.00185	.00179
Youngstown	.00567	.00567	.00599	.0118	.00728
Oklahoma					
Cherokee County*	.00024	.00024	.00008	.00022	.0002
Oklahoma City	.00176	.00176	.00108	.00122	.00146
Tulsa	.00086	.00086	.00041	.00068	.0007
Oregon					
Curry County*	.0001	.0001	.0001	.00012	.00011
Portland	.00293	.00293	.00104	.00626	.00329

(continued)

TABLE 10 (Continued)

CONCENTRATIONS OF BENZO(A)PYRENE IN THE AMBIENT AIR, 1966 ($\mu g/m^3$)

Location	1st Quar.	2nd Quar.	3rd Quar.	4th Quar.	Yearly Avg
Pennsylvania					
Clarion County*	.0017	.0017	.00066	.00172	.00145
Lancaster	.00176	.00176	.00032	.00522	.00227
Philadelphia	.0041	.0041	.00158	.00536	.00379
Pittsburgh	.00608	.00608	.00527	.00203	.00487
Reading	.00207	.00207	.00063	.00437	.00229
Warminster	.0009	.0009	.00018	.00176	.00094
Westchester	.0009	.0009			
Puerto Rico					
Bayamon	.0005	.0005	.00014	.00074	.00047
Guayanilla	.00027	.00027	.00018	.0014	.00053
Ponce	.0005	.0005	.0005	.00095	.00061
San Juan	.00149	.00149	.00041	.0009	.00107
Rhode Island					
Providence	.00284	.00284	.00144	.00743	.00364
Washington County*	.00028	.00028	.00022	.00032	.00028
South Carolina					
Columbia	.00239	.00239	.00045		
Greenville	.005	.005	.00081	.00918	.005
Richland County*	.00212	.00212	.00018	.00046	.00122
South Dakota					
Black Hills Forest*	.00012	.00012	.00016	.00018	.00015
Sioux Falls	.00095	.00095	.00054	.00077	.0008
Tennessee					
Chattanooga	.00621	.00621	.00167	.0193	.00835
Memphis	.00081	.00081	.00077	.00423	.00166
Nashville	.00545	.00545	.00117	.00981	.00541
Texas					
Dallas	.00113	.00113	.00131	.00189	.00137
Houston	.00099	.00099	.00063	.00095	.00089
Matagora County*	.00028	.00028	.00026	.00044	.00032
Pasadena				.00122	
San Antonio	.00041	.00041	.00032	.00104	.00055

TABLE 10 (Continued)

CONCENTRATIONS OF BENZO(A)PYRENE IN THE AMBIENT AIR, 1966
($\mu g/m^3$)

Location	1st Quar.	2nd Quar.	3rd Quar.	4th Quar.	Yearly Avg
Utah					
Ogden	.00014	.00014	.00041	.00149	.00055
Salt Lake City	.00018	.00018	.00005	.00455	.00124
Vermont					
Burlington	.00113	.00113	.00050	.00041	.00079
Orange County*	.00136	.00136	.00036	.00068	.00094
Virginia					
Danville	.0014	.0014	.00086	.00905	.00318
Norfolk	.00216	.00216	.00041	.00662	.00284
Shenandoah Park*	.00132	.00132	.00032	.00068	.00091
Wisconsin					
Door County*	.00028	.00028			
Milwaukee	.00617	.00617	.00131	.00275	.00410
Wyoming					
Cheyenne	.00054	.00054	.00037	.00063	.00052
Yellowstone Park*	.00006	.00006	.00002	.00008	.00006

*Indicates nonurban areas.